Diet Slows Brain Growth of 2 Million Children

Medical Tribune Report

NEW YORK—A California research team outlined here what it called "strong statistical evidence" that the brain development of over 2 million U.S. children is in jeopardy because of poor nutrition before or after birth.

The investigators also reported that infants and children of families living below the poverty level of income have, in the aggregate, unexpectedly small head circumferences."

Dr. Robert B. Livingston, of the University of California, San Diego, School of Medicine, said he and colleagues reached these conclusions after analyzing information gathered by two major nutrition surveys conducted in 1968-1970.

One of these—the so-called Ten State Nutrition Survey—was made by divisions of the Center for Disease Control, while the other was carried out collaboratively by Ohio State University and the University of Georgia.

Levels Established

The California group began its statistical study by independently establishing levels of nutrition intake "below which we had reason to believe there would be serious jeopardy to brain development affecting the unborn, the infant, and the young child," Dr. Livingston explained at the fifth annual meeting of the Society for Neuroscience.

The levels selected were those below which 97.5% of all normally healthy individuals are known to manifest growth retardation (in children) and weight loss below normal levels (in adults).

The research team then applied these criteria to the survey findings. Thus, pregnant women and children were considered in jeopardy for brain development if they were ingesting below 70% of their Recommended Daily Allowance (RDA) for energy and less than 40% of their RDA for protein, since these percentages are at levels two standard deviations below average requirements for such nutrients.

"It was found that nearly 60% of pregnant women living in poverty were, as of 1970, in serious jeopardy for the brain development in their unborn children due to their low total energy intake," Dr. Livingston reported.

Analysis of data from the surveys also indicated that 14% of pregnant women living in poverty fulfilled the "jeopardy criteria" for protein intake as well as energy requirement.

Malnourishment proved considerably less common among infants and young children. Of those under the age of four determined by the Ten State Survey to be living in poverty, 18% were categorized by the California group as being in jeopardy with respect to energy intake.

Dr. Livingston emphasized that malnutrition of both pregnant women and children was prevalent even among those at income levels two to three times that of the acknowledged poverty level.

If the percentages of pregnant women considered in jeopardy in the two surveys are projected for all pregnant women in the United States as a whole in 1970, the California group estimates that nearly 244,000 of those living in poverty, and about 700,000 others at near-poverty levels, had energy intakes below the level believed to jeopardize brain development of the fetus.

A similar projection nationwide for the Ten-State percentages of infants and young children adds up to nearly 1,177,000.

Small Heads

The finding that many infants and children from low-income families examined during the two nutrition surveys had small head circumferences was cited by Dr. Livingston as "perhaps the most compelling evidence" for the conclusion that undernutrition jeopardizes brain development.

Head circumferences for the poverty and near-poverty populations were compared with standard growth percentiles, he said. In a population meeting standards for normal growth, three per cent would be found below the third percentile, 10% below the 10th percentile, etc.

But among the surveyed infants and children living below the poverty level, 17.3% were found below the third percentile, and one-third were below the 10th percentile.

"Since head circumference correlates with brain volume, the smaller head circumferences reflect smaller brain dimensions," Dr. Livingston said. "This observation implies confirmation of the prediction from nutrition intake data that there are likely to be a large number of infants and children whose brain development was thwarted by undernutrition."

NIH Center Seeks Patients With Hemoglobinopathies

Medical Tribune Report

BETHESDA, MD.—The cooperation of physicians is requested in the referral of patients with various hemoglobinopathies, particularly sickle cell disease, cardiac hemolytic anemia, transfusional hemosiderosis, or thalassemia, for clinical studies into the pathophysiology of these disorders and treatment at the NIH Clinical Center here.

Physicians interested in having their patients considered for admission may telephone Drs. Arthur W. Nienhuis or Robert M. Winslow at (301) 496-3676.

Medical Tribune and Medical News

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Vol. 17, No. 5 world news of medicine and its practice—fast, accurate, complete Wednesday, February 4, 1976

No Occupational Exposure

Airborne Fibers Pose Threat of Asbestosis to All

Medical Tribune Report

CHICAGO—Ten cases of chronic pleural thickening, found in routine x-rays of asymptomatic men not occupationally exposed to asbestos, have been attributed to environmental asbestos exposure by a Navy radiologist.

Radiologically and pathologically, the lesions are identical to those of patients with proven asbestosis from occupational exposure.

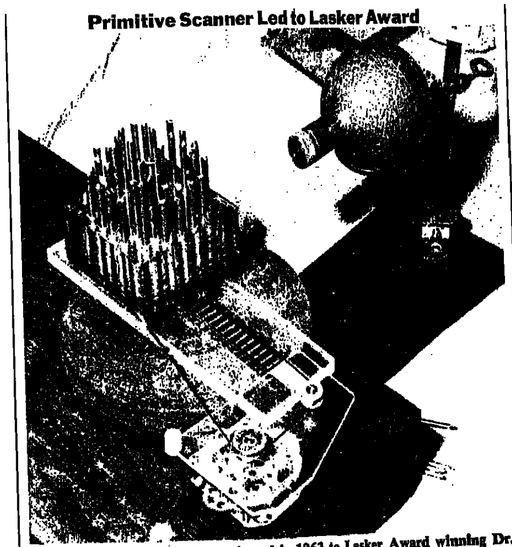
"It is our impression that the majority of people in the United States may have asbestos fibers in their lungs due to the widespread and increasing use of asbestos during the past three decades," said Capt. Charles W. Ochs of the Naval Medical Corps, Bethesda, Md. He estimated that 5% "may have tissue changes."

Although the first cases of pulmonary fibrosis due to inhalation of asbestos were reported in 1929, it was not until 1968 that epidemiologic studies established the role of asbestos in the development of lung cancer in cigarette-smoking asbestos workers.

"It is anticipated that the number of pleural thickenings will be more frequently seen in the future," said Dr. Ochs in an interview at the meeting of the Radiological Society of North America. "The list of asbestos uses is impressive and growing. It is used in cardboard, tiles, gutters, drain pipes, electrical insulation and a wide variety of other building materials. Vinyl asbestos floor tile also may be a significant source of airborne fibers. The major source is the automobile (brake linings, clutches, transmissions)."

Continued on page 48

Primitive Scanner Led to Lasker Award



U.S. Patent No. 3106,640 was issued in 1963 to Lasker Award winning Dr. William Oldendorf of Los Angeles for a device made from a gamma beam source, nails, HO track and a turntable—which demonstrated the basic system utilized, years later, in the British-created EMI scanner. Viewed by radiologists as "a toy," it was turned down by industry as unmarketable. See page 13.

1st Time Without Brain Regulation

Conditioning Effects Control Of Bladder Despite Cut Cord

Medical Tribune Report

ATLANTA—Bladder function control was successfully achieved, at least temporarily, in two patients with completely transsected spinal cords using classical conditioning techniques, Laurence P. Ince, Ph.D., senior psychologist, department of rehabilitation medicine, Goldwater Memorial Hospital, New York University Medical Center, reported here.

"This was, to our knowledge, the first successful conditioning of a re-

Continued on page 44

In Exclusive Interview with Dr. Sackler:

FDA Chief Labels Some Criticisms as Unfair

Cites Package Insert's Role

Medical Tribune Report

WASHINGTON, D.C.—How the practicing physician should consider the package insert was one of the major points discussed by Federal Drug Administration Commissioner Alexander M. Schmidt in an exclusive interview with Dr. Arthur M. Sackler, International Publisher of MEDICAL TRIBUNE.

The package insert's purpose has been misunderstood and criticism of the FDA as "behind the times" is unfair and erroneous, asserted Dr. Schmidt in an effort to clarify the in-

Continued on page 44

Vicki Lambert Photo

DR. ALEXANDER M. SCHMIDT

Text of Interview: Part II

Q. I believe you wanted to clarify for the practicing physician the role of the package insert. What are the principal misunderstandings in this respect in your opinion?

A. They are easily illustrated by some articles that have been appearing recently, and by criticism directed at the agency, both claiming that the package insert is "behind medical practice." It has been pointed out, for example, that the labeling for propranolol does not include hypertension as an indication.

Continued on page 12

As Early as Age 5

Higher BPs in Black Pupils Than in White

BY NATHAN HORWITZ
Medical Tribune Staff

ANAHEIM, CALIF.—Black children have significantly higher blood pressures than white children, starting as early as age 10, and these higher pressures may even occur by age five, a Louisiana State University team has reported.

The finding, believed to be the first to document elevated blood pressures among black youngsters, compared to whites in the same age group, was based on a federally-funded study of virtually all schoolchildren, aged five to 14, in the bi-racial community of Bogalusa, La., according to Dr. Antonie W. Voors, Associate Professor of Preventive Medicine.

Racial differences in blood pressure occurred significantly at every age among those in the upper five percentiles of the BP groups, and these differences were present, although not at statistically significant levels, in the lower percentiles, Dr. Voors told the annual meeting of the American Heart Association.

Most of the children (95% of the black and 91% of the white) in Bogalusa and its immediate area participated in the continuing study. The investiga-

Continued on page 6

Inside this issue of

sexual medicine today

Dr. Robert L. Dickinson: 'Facts must be sought that facts may be taught'—Prestigious in medical circles and a religious man, Dr. Dickinson nonetheless defied Victorian taboos to search for the truth about sexuality. Part I.

Hazards of sexually transmitted diseases (STD)—Important clinical aspects of some of the newly recognized forms of STD, of special interest to family practitioners. Authorities in the field outline measures to combat them.

Show us! Coping with *Show Me! A Picture Book of Sex for Children and Parents*—German Sex authority Dr. Claus Wiedeking pans and praises this controversial book, translated from the German and "edited" for U.S. readers...

Open to page 13

Restricted Approval Expected For Injectable Contraceptive

By ALAN FITZGIBBON
Medical Tribune Correspondent

ROCKVILLE, MD.—Medroxyprogesterone acetate, the long-term injectable contraceptive, may go on the market after all.

The drug has twice been on the verge of restricted sale as a contraceptive, but each time its marketing was held up by doubts about its safety.

Now a subcommittee of the Food and Drug Administration's Obstetric and Gynecology Advisory Committee has concluded that certain methodologic problems in testing the agent's safety are irresolvable without marketing. It has recommended that the drug be prescribed for only a limited group of patients and that its use be controlled through a registry system.

For The Incapable

Patients for whom medroxyprogesterone acetate could be prescribed would be those who refuse or are unable to accept the responsibility demanded by other contraceptive methods, such as retardates; who are incapable or unwilling to tolerate the side effects of conventional oral contraceptives; and in whom other contraceptive methods have repeatedly failed. Only physicians could authorize the use of the drug, and pharmacies would report prescriptions to the manufacturer which in turn would make cumulative use data available to the FDA.

The subcommittee's recommendation, which was discussed at a recent all-day meeting of the parent advisory committee here, will now undergo further study by the FDA staff and consideration by Dr. Alexander M. Schmidt, the FDA commissioner, before a final decision is reached.

If Dr. Schmidt does allow medroxyprogesterone acetate to be marketed as a contraceptive, it is unlikely that his decision will settle the doubts that have surrounded the drug for more than two years.

The agent was first approved by the FDA as an experimental contraceptive a decade ago, and since then has been used by about 1,000 women annually in the United States and several times as many abroad. It has also been approved for use in treating uterine cancer.

In October, 1973, the agency announced provisional approval of the drug as a 90-day injectable contraceptive for "a small but definable group of women," meeting the same criteria as those the subcommittee now recommends.

Approval Postponed

After the several required months of public comment on its proposal to approve, the FDA was ready to grant final marketing approval in early April 1974. It suddenly postponed that step, however, when the staff of Rep. L. H. Fountain's House Intergovernmental Relations Subcommittee publicized an "extremely important" disclosure.

That data published by the National Cancer Institute in 1971 showed a cervical carcinoma *in situ* rate which was several times higher in medroxyprogesterone acetate users than in women generally.

In fact the FDA was aware of the data and had placed it under consideration. However, for technical reasons the agency had decided that the data could not be extrapolated to the particular problem at hand.

After further study of accumulated experimental data within the FDA, Dr. Schmidt announced in September, 1974 that a final order would be published the following October 12 approving the drug for contraceptive use along the lines announced a year earlier.

Re-enter Representative Fountain. Ten days before medroxyprogesterone acetate was to be licensed, the House subcommittee chairman wrote Casper W. Weinberger, then Secretary of Health, Education, and Welfare, that the drug might "irreparably injure" users. Final approval was again postponed for further study.

Among other things, the congressman said in his letter that:

- An FDA statistician had noted in a memorandum several months earlier that the incidence of cervical cancer in situ was three times higher among white women and 2.6 times higher among nonwhite women given the drug in the standard dose, and that it was 9.9 times higher among whites and 4.8 times higher among nonwhites when the standard dose was supplemented by estrogen.
- The director of the FDA's Office of Scientific Evaluation had urged further studies of the agent's possible carcinogenicity in another memorandum. He was particularly concerned about data linking the drug with breast cancer in female beagles, which had caused the FDA to prohibit its use in oral contraceptive formulations.
- The FDA seemed intent on approving medroxyprogesterone acetate for conception control "regardless of the insufficiency of available information" about its possible hazards.

In the wake of the FDA's second backoff, its Obstetric-Gynecology and Biometric-Epidemiological Methodology Advisory Committees met for two days last April to review the agent's safety once again. Among the problems before the panel were to determine the incidence of cervical carcinoma in situ among the drug's users, to decide whether the cervical cancer data in the National Cancer Institute's earlier epidemiologic survey could be compared with those in the new drug application for the agent—a question resulting from Mr. Fountain's letter, and to determine what further studies might be needed to settle the drug's possible carcinogenicity. After hearing various reports, the two advisory committees voted to turn these and other questions about medroxyprogesterone acetate over to a joint subcommittee and consultants for further examination.

Among the several reports the committees heard were one by Bertram D. Litt, the FDA statistician whose June 17, 1974, memorandum about above-

Continued on page 51

Aid for Eyeglasses

Lightweight, self-adhering membrane prisms, developed by Optical Sciences Group, Inc., are designed to correct strabismus and double vision. Prisms can be peeled off of glasses, replaced as needed.

Rape Clues Seen In Seminal Fluid, Sperm Marker

By JOHN HENAHAN
Medical Tribune Correspondent

LOS ANGELES—Two biochemical clues that could prove useful in rape cases have been uncovered by Dr. George F. Sensabaugh and his colleagues in the Forensic Science Group, School of Public Health, University of California at Berkeley.

The first is an enzyme which is found in the semifinal fluid, while the other is a genetic marker in the sperm which appears to vary according to hereditary background, Dr. Sensabaugh told the 1975 Conference on Chemistry and Spectroscopy here.

The seminal enzyme is one of the acid phosphatases. Even though its chemical and immunologic properties are similar to other tissue acid phosphatases, the enzyme found in semen has its own unique characteristics when separated by gel electrophoresis, he said.

Three Genetic Markers

Analysis of the electrophoretic patterns of acid phosphatases, with molecular weights ranging from about 100,000 to 125,000, showed characteristic bands in the seminal acid phosphatase patterns which were not found in the enzymes from other tissues, Dr. Sensabaugh told MEDICAL TRIBUNE.

Although acid phosphatase has been used in the past as presumptive evidence of sperm in rape cases, it is not unequivocal proof, since the enzyme is also secreted naturally in the vaginal tissue. Now that the enzyme difference in the seminal fluid has been detected, it should be easier for forensic scientists to determine whether or not rape may have occurred, he explained.

In another phase of the Berkeley research, Dr. Sensabaugh and E. F. Blake have identified three different "genetic markers" in the sperm of 55 donors. Unlike genetic markers found in other tissues, including the blood, the sperm markers appear to be unique, Dr. Sensabaugh asserted.

Continued on page 50

index

CLINICAL NEWS NOTE: *"It is of significance that conditioning was achieved in the absence of brain regulation. It is the first such instance involving human subjects. Until this time, cognition had been considered essential for any conditioning to take place. However, since both subjects had a complete transsection of the cord, cognition is ruled out as an intervening variable."* (Laurence P. Ince, Ph.D., senior psychologist, department of rehabilitation medicine, Goldwater Memorial Hospital, N.Y.C. See page 1.)

feature index

Medical Tribune

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EDITORIAL CAPSULES

. . . brief summaries of editorials or comments in current medical and scientific journals.

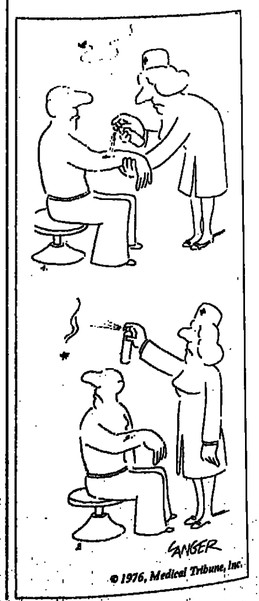
Epidemic on Wheels

". . . Statistics from three Latin-American countries, Chile, Costa Rica and Venezuela, reveal that, as in the U.S., traffic accidents have become the leading cause of death among young adults.

"About 250,000 people throughout the world are killed in traffic accidents each year, and more than seven million are injured. Although the U.S. has the highest number of people killed in traffic accidents of any country (about 50,000 per year), it has one of the lowest rates of fatalities per motor vehicle or passenger mile. For example, in the U.S. there are six fatalities per 100 million passenger miles, whereas in Kenya and Uganda there are from 55 to 65 fatalities per 100 million passenger miles. In India the fatality rate per motor vehicle is 10 to 15 times higher than it is in the U.S. In all countries the death rate from traffic accidents is higher for males than it is for females.

"The majority of developing countries have a higher incidence of traffic accidents involving pedestrians than of accidents involving motor vehicles alone. Among the causes, the WHO reports, are poor roads, pedestrian ignorance of road signs, lack of instruction in the use of roads and heavy pedestrian and bicycle traffic on the roads.

"To combat the growing epidemic of traffic accidents, the WHO has undertaken a worldwide epidemiological study of road traffic accidents and [is] encouraging the development of preventive programs. . ." *(Science and The Citizen, Sci. Amer. 234:56, Jan., 1976)*



Aspirin Controls Diarrhea In Uterine Ca Radiotherapy

By FRANCES GOODNIGHT
Medical Tribune Staff

LONDON—Aspirin given four times a day to patients undergoing radiotherapy for uterine cancer "effectively controlled" the therapy's side-effects of diarrhea and other gastrointestinal symptoms in almost all of the women taking part in a clinical trial conducted here at Royal Marsden Hospital.

Publication of the study's findings, however, led an investigator from London's Central Middlesex Hospital to urge caution in using aspirin to suppress these acute symptoms since it "may allow the continued irradiation of patients otherwise too ill to withstand further treatment."

14 Patients Studied

The double-blind, balanced, and randomized trial of aspirin included 14 patients who took highly buffered acetylsalicylate and 14 who received the equivalent effervescent antacid buffer without aspirin over a 72-hour period. All had experienced an increased daily number of bowel motions after the beginning of irradiation for uterine cancer and many were also affected by abdominal pain, flatulence, or nausea.

Describing the trial outcome in *Lancet* (Nov. 5, 1975), Dr. A. T. Mennie and colleagues said that 11 of the 14 treated with aspirin reported a reduction in the number of bowel motions. By comparison, only three of the 14 controls had lessened diarrhea.

The women taking aspirin also obtained relief from the other side-effects of irradiation. Of the eight in this group who had had colicky abdominal pain, all were relieved whereas none of the seven controls was helped.

Similarly, all patients on aspirin who had complained of flatulence and/or nausea became symptom-free.

The Royal Marsden investigators believe the findings "support our view that the gastrointestinal symptoms following radiotherapy are caused by excessive production of prostaglandins, probably in loops of gut exposed to radiation."

It is thus probable that acetylsalicylate acts by inhibiting this prostaglandin production, they said. Citing a report from another research center, they noted that blood levels of prostaglandins are increased in rats exposed to whole-body irradiation.

In their opinion, evidence is also available that aspirin or other inhibitors of prostaglandin biosynthesis may control diarrhea brought about by causes other than radiation. As one example, they pointed out that the stools of patients with ulcerative colitis contain increased amounts of prostaglandins, and that an effective remedy is sulphasalazine—a known inhibitor of prostaglandin biosynthesis.

Intestine Irradiated

The call for caution in the use of aspirin to suppress symptoms produced by pelvic irradiation was sounded in a follow-up letter to *Lancet* (Nov. 22, 1975) by Dr. R. E. Pounder, of Central Middlesex Hospital.

Acute intestinal side-effects arise in only a small proportion of women undergoing radiotherapy for uterine carcinoma but they indicate that the intestine is being irradiated, Dr. Pounder said.

"I have the impression that the patients who develop severe symptoms during pelvic radiotherapy are those who may subsequently develop chronic ill health, or even die, from damage to their intestine," he commented, adding that diarrhea during the course of such therapy "is a warning which should result in the treatment being reviewed, replanned, or stopped."

Because aspirin is freely available, Dr. Pounder summed up, there is the risk that it will be widely administered for this indication before long-term studies have been made. Until more information is available, he advises that aspirin "should generally be given to patients only after the cessation of pelvic irradiation."

. . . But Radiologists Advise Caution Lest Dose Intolerance Be Masked

NEW YORK—Asked by MEDICAL TRIBUNE to evaluate these British reports on use of aspirin to relieve side-effects of radiation in uterine cancer patients, a New York radiologist called the study's findings "a valuable contribution."

But Dr. Charles Botstein, Professor of Radiology at Albert Einstein College of Medicine, emphasized the importance of the cautionary point made in the subsequent letter concerning the significance of severe symptoms.

"Almost all such patients have a certain degree of mild diarrhea but this is usually very transient and mild," he said.

"If it becomes so severe that it requires treatment, then this is an indication that the rectum doesn't tolerate radiation well and that you might see a late complication in the patient. By using aspirin as a stratagem to block diarrhea, you would rob yourself of a guiding light."

Citing management at his hospital, Dr. Botstein said that in any case where antidiarrhea medication proves necessary, this is considered a warning sign, and the treatment plan for that patient is reviewed carefully. It is then modified to reduce the dose of radiation to the rectum unless a high dose is unavoidable for the patient to survive.

Significant complications of the radiation have an acceptable occurrence rate of about 5%, he noted, and include stenosis, bleeding from the rectum, and occasionally a contracted bladder.

"An experienced doctor knows that you do not see such complications in patients who did not have diarrhea during radiation treatment," Dr. Botstein commented. "If the patient did experience severe diarrhea, then you can expect late complications."

In instances where a patient does develop stenosis or a perforation in the rectum or sigmoid years after treatment, he added, "look back in the history and you will find that she had severe diarrhea during radiation."

Dr. Botstein believes that aspirin should not be given prophylactically, since this would reduce the physician's ability to assess treatment effects and to guard against production of complications. It can be given, he said, once the situation has been evaluated and the treatment has been adjusted to reduce the radiation dose to the rectum.

Effect on Tumor

► Raising a different point, Dr. Basil Hilaris, of the Memorial Sloan-Kettering Cancer Center, said he is concerned with "what is happening to the tumor" when aspirin is taken at the time of radiation treatment.

The findings from the British study are sound and well-supported, Dr. Hilaris agreed. But in his opinion, it must be asked whether the dose of radiation planned for a given patient with cancer of the uterus or cervix would be as effective as expected if she is also receiving aspirin.

"We need more basic laboratory work, more clinical studies, to determine how the agent affects both the tumor and normal tissues," he said.

Computerized Therapy

UCLA computer plots direction and depth of radiation beams in Ca therapy; doctors in remote areas plug in via computer terminal.

Drunk Truckers Escape Charges In Road Mishaps

Medical Tribune Report

SAN DIEGO—Although about half of the tractor trailer drivers who are killed in road accidents may have had excessively high blood alcohol levels, only about 2% of tractor trailer drivers held responsible for fatal accidents were charged with drunk driving, according to a study recently completed at the Johns Hopkins School of Hygiene and Public Health.

The discrepancy between the two statistics might be bridged if federal standards that now call for blood alcohol tests for all drivers involved in crashes fatal to other persons were fully implemented, said Susan P. Baker, President of the American Association for Automotive Medicine at its 19th annual meeting.

"Collisions involving tractor trailers are of special interest because they are more likely to have serious consequences than most other motor car crashes. This is largely a reflection of the inability of present vehicles to protect their occupants against the tremendous forces generated by such accidents," she said.

In the Johns Hopkins study, a series of 150 fatal crashes that occurred on Maryland highways and which involved tractor trailers was studied retrospectively. Twenty-five tractor trailer drivers and 63 drivers of other vehicles died and were tested for alcohol. About one third in each group had blood alcohol concentrations of 0.1% by weight or more. Of 17 tractor trailer drivers apparently responsible for crashes, eight had illegal alcohol concentrations. However, only 2% of the surviving drivers were charged with driving while intoxicated or impaired, Mrs. Baker pointed out.

"The role of alcohol has not been adequately examined in fatal crashes involving tractor trailers," she asserted. "Although research based on police reports indicates that drivers of heavy trucks involved in fatal or other crashes are rarely intoxicated, alcohol information from police reports usually is based on the officer's impressions rather than chemical tests."

To reduce the level of accidents involving tractor trailer drivers who have been drinking (most of whom appear to be short haul drivers), Mrs. Baker recommends that persons applying for licenses to drive the huge rigs should be carefully screened to determine whether they have alcohol problems.

She also recommends:

- Giving blood tests to drivers at weigh stations when there is a suspicion of drinking. Employers might also do the same before sending a driver out.
- Compulsory blood tests, including surviving drivers, as soon as possible after fatal crashes.
- Information from the National Driver Registration indicating a history of drunk driving should be made available to help companies screen out potentially hazardous drivers before they are employed.

Beef-Vitamin Diet Prevents Protein Loss

CAMBRIDGE, MASS.—Feeding seriously ill, hospitalized patients a special diet consisting of lean beef, vitamins, and minerals (400 to 700 calories/day) could help protect them against debilitating protein losses that occur during infection, according to researchers at the Massachusetts Institute of Technology and Harvard Medical School.

An open letter to the doctors of America

Subject: **The all-important physician-patient relationship**

Dear Doctor:

We must and will do something about it.
The science and art of medicine has reached its most advanced state but the all-important physician-patient relationship is plunging to an all-time low.

We must do something about it.
The establishment of "cost-effective" control rather than "therapeutic-effective" practice is part of the drive towards the government's dominance, if not takeover, of medicine. Physicians personally, and the medical profession generally; medicines specifically, and diagnostic and other procedures generally, have become a target for governmental attacks as a result of the pressures generated through sensation-seeking consumerism and political expediency.

Patient regimens are too often disrupted, medical advice disregarded and medications neglected. Early diagnosis of essential conditions is being placed in jeopardy and early treatment delayed.

We must do something about it.
Medical Tribune has addressed these issues editorially. Medical Tribune has encouraged the mobilization of official bodies of medicine. It has reported extensively on constructive efforts by *ad hoc* committees of physicians. We have discussed these problems at great length with responsible consumer leaders, leaders in all fields of medicine, and with a whole gamut of government officials.

More is needed.
Medical Tribune has developed and is introducing an innovation in patient education to help rebuild and sustain the all-important physician-patient relationship. Medical Tribune has prepared a series of supplements for use in physicians' waiting rooms, clinics, and hospitals, entitled THE GOOD DRUGS DO. Each supplement is prepared by an outstanding leader in one of the fields of medicine. Each supplement is written so that the patient can understand it. Each seeks to advance the goal of an informed patient, a cooperative patient, and a patient confident in his physician's practices, medicines and recommendations. The waiting room patient supplement, THE GOOD DRUGS DO, will be coming to you as a section of Medical Tribune.

THE GOOD DRUGS DO patient supplement in Medical Tribune seeks to do something positive about the physician-patient relationship.

THE GOOD DRUGS DO supplements prepared thus far consist of a general introduction by Dr. Louis Lasagna, covering the broad advance made by therapeutic medicine in the Golden Age of Therapeutics. THE GOOD DRUGS DO individual supplements then go on to take up Depression, Hypertension, Nutrition and Vitamins, Alcoholism, Diabetes, Arthritis, Psychoses, Antibiotics. Each subject supplement is prepared by an outstanding authority in the field and addressed to patients.

Please remove THE GOOD DRUGS DO supplements from coming issues of Medical Tribune and put them in your waiting room.

You can help us help your patients by making this essential material available to them and by advising us as to how we may make improvements in your and your patients' interests.

We can do something about the all-important physician-patient relationship.

Sincerely,

International Publisher

Coming in the next issue: **THE GOOD DRUGS DO in Depression**

Higher BPs Found In Black Children Than in White

Continued from page 1

tion is part of the Bogalusa Heart Study, funded by the National Heart and Lung Institute, and designed to help identify the early risk factors in the natural history of atherosclerosis.

All children received nine blood pressure readings by trained observers using both sphygmomanometers and automatic blood pressure recorders in a randomized design, Dr. Voors reported. He stressed that a special effort was made to create a relaxed and tranquil atmosphere in which to take the readings. As a result he said, the basal BP measurements for the group were somewhat lower than those reported for school-age children in other investigations.

The study population was divided into groups based on increments of 5% in increasing blood pressure readings. Analysis of the data, Dr. Voors reported, showed that the black schoolchildren had "significantly higher blood pressure" than the whites, and that "this racial difference was largest in children in the upper 5% of the blood pressure ranks."

Automatic Method Better

The two instruments employed in the study—the mercury sphygmomanometer and the automatic blood pressure recorder—gave somewhat different overall results, with the automatic instrument detecting racial differences in BP levels starting at age five, while the sphygmomanometer showed these differences only in the 10-to-14-year-old group. In an interview, Dr. Voors told MEDICAL TRIBUNE that the automatic instrument appeared to be significantly more accurate and sensitive than the sphygmomanometer.

A breakdown of the data, he continued, showed that at the 95th percentile, in every age, the mean systolic pressure for black youngsters was 5 mm higher than that for the whites, and the mean diastolic about 4 mm higher than that for whites. In the other percentiles, the differences were smaller, "on the order of a mean of 1-3 mm between black and white subjects, depending on the instrument used."

In other findings, he reported, the child's height and the combination of height and weight appeared to play a greater role in determining elevated blood pressures than increasing age. Thus, taller and more obese children were likely to show elevated blood pressures at an earlier age than shorter and/or thinner children.

Saving on Drug Costs

Medical Tribune Report

PHILADELPHIA—Consumers who patronize chain drugstores are conservatively estimated to have saved $200 million in prescription costs in 1974, according to a Wharton School study, which found that chain drugstores charge substantially lower prices than independents for identical prescription drugs.

Current Opinion

Pro and Con on Dr. Lasagna's Letter and Dr. Sackler's Column

From One Who Takes the Same Position as Dr. Lasagna and Dr. Sackler.

LEO J. GEPPERT, M.D.,
Director, Alamo Blue Bonnet Unit
San Antonio State Hospital,
San Antonio, Tex.

I AGREE COMPLETELY with Dr. Lasagna and Dr. Sackler. I am enclosing excerpts from a paper, "Composition of Pediatric Practice at a Permanent Army Base in the Antibiotic Era," (*Pediatrics* 22:336, Aug. 1958) which provides statistical information to support your view.

"Respiratory infections including otitis media and cervical adenitis accounted for 52% of all illness, but less than 5% of all deaths (11% of pediatric deaths).

The reaction of medical students and interns to outpatient pediatric experience is usually that pediatric practice consists chiefly of treating "runny noses." Although it is true that about 16% or almost one out of five "sick patients" have nothing more definite than coryza, the American mother is thereby much maligned. She does not run to the doctor each time her child has a cold. Children have at least six respiratory infections a year (*New England J. Med.* 252:1066, 1955), but were brought to the clinic only twice in 10 years when nothing else was disclosed by physical examination. Two times out of three the mother was correct in her apprehension. A diagnosis of a more severe respiratory disease was made 6,000 times per 1,000 children—simple coryza only 2,000 times per 1,000 children during the first 10 years of life. Furthermore, almost 1% of children with a common cold seeking medical attention were deemed sick enough to require admission to the hospital. That croup remains a constant threat to life is evident in our mortality statistics."

". . . Only the common cold and acute pharyngitis or tonsillitis occurred in every child. These common upper respiratory infections accounted for 40% of all illnesses, but only 8% of hospital admissions and no deaths" (See Table III).

TABLE III

Diseases Due to Lower Plant or Animal Parasite

*(for the incidence per 100,000 children under 10 years of age per year)**

	Outpatient Morbidity	Inpatient Morbidity	Newborn Morbidity NB	Deaths Ped.
Respiratory System				
Tonsillitis, or pharyngitis, acute	24,921	512		
Common cold	19,928	183		
Bronchitis or tracheitis, acute	3,686	222		
Bronchopneumonia ("pneumonitis")	1,622	581	15	5 13
Sinusitis, acute	844	82		
Laryngitis, acute	377	54		
Tuberculosis, primary	243	39		
Bronchiolitis	144	46		1
Sinusitis, chronic	130	7		
Primary atypical pneumonia	128	29		
Pertussis	110	59		
Laryngotracheobronchitis	101	82		3
Bronchitis, chronic	45	15		
Pneumonia, lobar	41	21		
Pneumonia, interstitial, acute	24	24		
Bronchiectasis	20	7		
Atelectasis, due to infection	10	6		
Pleurisy, acute	6	4		
Pyopneumothorax, staphyococcus	5	5		
Emphysema, lobar	4	4		
Abscess, lung	4	4		
Diphtheria	3	3		
Papilloma	3	3		
Total	52,399	1,992	15	5 17

*Figures represent incidence for pediatric population of 10,000 during a 10-year period. Data gathered by Dr. Geppert when he was Chief, Pediatric Service, Brooke Army Hospital and later as Theater Consultant in Pediatrics, A.F.F.E.

"Uncommon Colds" and Antibiotics: Not Good Enough for Either the President Or the Citizens of the United States

ALBERT B. SABIN, M.D.
Distinguished Research Professor of Biomedicine
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IN THE NOV. 19, 1975, MEDICAL TRIBUNE Dr. Arthur M. Sackler discussed the old question of the misuse of antibiotics in the treatment of the "common cold" and "uncommon colds." Based largely on a Mar. 27, 1974 letter from the distinguished pharmacologist, Dr. Louis Lasagna, [printed in MT Nov. 19 and 26, 1975] Dr. Sackler concluded that practicing physicians were using antibiotics therapeutically to treat "uncommon colds" defined as secondary bacterial complications of the "common cold" rather than prophylactically for the prevention of secondary bacterial complications of the vast amount of acute respiratory disease of multiple etiology.

The impression I gathered from Dr. Sackler's Nov. 19 article and from the Nov. 26 editorials is that the problem stems from continuing "attacks on the medical profession by government officials, including top doctors in FDA and HEW . . . Prominent among the charges of professional incompetence is the indictment that practicing physicians are misusing antibiotics for the 'common cold'."

Misuse Still A Problem

Dr. Sackler then reported that the treatment given the President of the United States included an antibiotic for his recent respiratory illness which consisted of "sinus congestion, a tendency to cough, and a temperature slightly above 100 degrees." If these clinical manifestations are indeed regarded by practicing physicians, including the President's physician, as indicators of secondary bacterial infection requiring antibiotic therapy, the extensive and potentially dangerous misuse of antibiotics by the medical profession throughout the world still presents a problem of professional concern.

In 1969, as president of the Infectious Diseases Society of America (and not as a top doctor in FDA, HEW, or even an "arm-chair medical general") I expressed the judgment of my colleagues when I said: "I wish to call attention once again to the misuse of bacterial antibiotics in the treatment of nonbacterial infections of the respiratory tract. These antibiotics are used by physicians all over the world in an attempt to prevent the complications caused by secondary bacterial infections.

"It is highly probable that a large proportion of the more than $750 million spent annually in the United States on anti-infective drugs is spent for this purpose. Several well-controlled studies showed that the use of antibiotics for this purpose is contraindicated, not only because they fail to diminish the incidence of secondary bacterial complications but also because the secondary infections that do occur are frequently caused by antibiotic-resistant bacteria that are very difficult to treat. Antibiotics should be used only after a secondary bacterial infection has been identified." (From Sabin, A. B.: Control of infectious diseases, *J. Infect. Dis.*, 121: 91-94, 1970. For review of many controlled studies see: Davis, S. D. and Wedgwood, R. J.: Antibiotic prophylaxis in acute viral respiratory diseases, *Am. J. Dis. Children*, 190: 544-553, 1965. See also editorial of Jordan, W. S., Jr.: Colds, drugs, and doctors, *Antibiotics and Chemotherapy*, 11: 371-372, 1961)

Our Area of Responsibility . . .

Leighton E. Cluff, president of the Infectious Diseases Society of America in 1973, said the following: "Antimicrobial drugs are of great importance and value, but they are costly, and everyone recognizes that they are overused and misused. Legislation, regulation, education, and other methods have not appreciably affected the improper use of antimicrobial drugs by most physicians . . . Is it justifiable for experts in infectious diseases, whether in an academic setting, industry, or practice, to be unconcerned about how antimicrobial drugs are used? If this is our area of competence and responsibility, can we reasonably ignore it?" (Infectious diseases: A perspective, *J. Infect. Dis.*, 129: 86-91, 1974).

The important issues really are how much acute nonbacterial respiratory disease is more than an "uncomplicated coryza" [see Dr. Lasagna's letter] severe enough to make people go to bed, what are the clinical indicators that a practicing physician may use to suspect primary or secondary bacterial infection, and then what to do to answer Dr. Lasagna's question: "what antibiotic would be best?".

Extent of Respiratory Illness

Acute respiratory disease is responsible for more millions of days of bed disability in the U.S.A. than all of heart disease, cancer, and stroke combined (Table 1). The classical Cleveland studies, summarized in the book, *'Illness in the Home'* by J. H. Dingle, G. F. Badger and W. S. Jordan, Jr. (The Press of Western Reserve University, Cleveland, 1964) showed that 62.7% of a total of 25,155 illnesses over a ten-year period in selected Cleveland families were made up of acute respiratory illness, and that 95% of the latter were in the category of "common respiratory diseases" which included the "common cold, rhinitis, pharyngitis, bronchitis, and other acute respiratory illnesses of undifferentiated types." Streptococcal tonsillitis and pharyngitis constituted only 2.77% of the 15,783 respiratory illnesses, nonbacterial tonsillitis and pharyngitis 1.39%, "primary atypical pneumonia" 0.25%, pneumonia (pneumococcal and other bacterial or un-

Continued on page 45

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"I'll see you again the week after next and we'll see how you're making out."

Your patient is often likely to feel reassured when you talk about seeing him again to check his progress. A planned visit evidences your continued interest and affords the patient an opportunity to report improvement he has made and to relate whatever continuing or additional difficulties he may be experiencing. It's also a chance for him to describe his response to therapy with Valium.

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Advances in Molecular Biology

JUST ABOUT 11 YEARS AGO, an editorial on this page, entitled "Advances in Molecular Biology," stated, "It seems likely that fragments of DNA, the segments we call genes, will be identified, whether directly in situ or indirectly, by recognition of their particular messenger RNAs."

Well, more than that was recently accomplished by four scientists at Harvard University. Argiris Efstratidis, Fotis Kafatos, Thomas Maniatis and Allan Maxam have synthesized the gene that is responsible for the formation of rabbit hemoglobin. They began with purified rabbit messenger RNA that directs cytoplasmic ribosomes to build hemoglobin. With the use of reverse transcriptase—the enzyme for which the 1975 Nobel prize was bestowed upon its discoverers, Drs. David Baltimore and Howard Temin—they induced the RNA to reverse its action and make a single strand of DNA from a *Gemisch* of precursor nucleotides. By the addition of DNA polymerase, a complementary strand of DNA was attached to the single strand. The double helical structure could be cleaved by a particular nuclease. Rabbit hemoglobin DNA contains about 650 nucleotide units, in the range of size of the human hemoglobin gene.

In 1970 and in 1973, Har Gobind Khorana and his colleagues at MIT reported the synthesis of double-stranded genes directing the formation of alanine and tyrosine. But these are much simpler structures and they were formed by complicated organic chemistry based on knowledge of known nucleotide sequences. What the Harvard investigators have done is of a different character and in line with the prediction made in the 1965 MEDICAL TRIBUNE editorial.

The 1965 editorial closed with the following remarks: "It would be rash to predict the outcome of these studies of the nucleic acids. The beginning of this century coincided with realization of the genius of Mendel and his genetic discoveries 35 years previously. The distance traversed since that time is extraordinarily far. Mendel's 'determinants' of traits became known as genes, located on chromosomes. We now know what the constituents of chromosomes are, how chromosomes replicate, and why genes *are* genes. We have identified the steps leading from DNA through the various RNAs to the formation of proteins. The code of the nucleotides is well on the way to decipherment. The structure of one of the simpler nucleic acids has been spelled out, and it will doubtless be synthesized as well. Who would have foreseen all this at the turn of the century? Who can foresee what the future holds?"

Clearly, it is now possible to make any double-stranded DNA once its purified RNA has been prepared. It should then be relatively simple with the use of available techniques to synthesize large quantities of particular genes. The ultimate direction taken by these advances in molecular biology remains uncertain.

Medical Education

IN 1930-31, there were 76 medical schools in the U.S. with a total enrollment of 21,982, the first-year class constituting 6,456 and the graduates of that year numbering 4,735. Fifteen years later, in 1945-46, there were 77 medical schools, with a total enrollment of 23,216, a first-year class of 6,060 and graduates numbering 5,826. But now that the war years were over, a remarkable expansion was to take place.

By 1974-75, there were 107 fully approved U.S. medical schools plus five with provisional approval and two offering approved basic science courses of the first two years. The total enrollment of these 114 medical schools was 54,074, the first-year class numbered 14,963 and the graduates that year were 12,714. There are 11 more medical schools in the planning stage but even without these additions, the 114 current schools expect to have a first-year class of 15,946 by 1979-80 and 14,999 graduates that year.

All this information is available in the education number of *J.A.M.A.*, the final issue of 1975. These remarkable achievements in the expansion of medical education must be related to the changes that occurred in our total population. The population of the U.S. in 1930 was about 123,000,000. Our current population is estimated at about 212,000,000. So our population has grown by about 72% since that time. Although the number of medical schools has increased by only 50%, the number of medical students has increased by 147% and the yearly graduates by 97%.

Blocking Radiotherapy's Side-Effects

CLINICAL QUOTE: *"Almost all [patients undergoing radiotherapy for uterine cancer] have a certain degree of mild diarrhea . . . If it becomes so severe that it requires treatment, then this is an indication that the rectum doesn't tolerate radiation well and that you might see a late complication in the patient. By using aspirin as a stratagem to block diarrhea, you would rob yourself of a guiding light."* (Dr. Charles Bolstein. See page 5.)

"This inferiority complex I've got... I assume it's not a very good one, is it?"

LETTERS TO TRIBUNE

Costa Rica Anyone?

Much has recently been written about Costa Rica and the many American "Pensionados" (retirees) who have settled there. Had it not been for a bout with breast cancer, we would already be among them. Because of the excellent medical facilities in Costa Rica, I have been given the okay for our move to Guanacaste Province, near Liberia City.

We will soon be building our home in Ranchos Maricosta, where we will have a few cattle for the freezer, horses for our two children, a garden, and fruit and nut trees. It is a long-awaited dream—and we can hardly wait!

Cost of living is still so low and taxes there so nearly nonexistent we can live comfortably on my husband's modest Navy retirement pay. We can hunt in the nearby mountains, fish in the Pacific and, if we ever tire of that, we can play golf and tennis, or just laze around in the sun (as we used to be able to do in now-many-times-more-expensive Hawaii).

If any readers would like more information about this beautiful, amazing little country and its Retirement Law, they can write me.

MRS. LEWIS M. BIRD
7000 South Dent Road
Hixson, Tennessee 37343

Meditating on Meditating

"Meditation without Metaphysics," (MT, Nov. 19) well summarizes the technique of transcendental meditation (TM).

The use of a mantra is an integral part of TM. It should be a meaningless word—otherwise it calls forth ideas which may disturb the orderly procedure. That is the reason why, I believe, the word "one" can serve only if it is pronounced to rhyme with "bone." Otherwise, one tends to lapse into counting—one—two—etc.

I have taken the standard course and believe that Dr. Herbert Benson has performed a service in making TM available without the trimmings. Incidentally, I have experimented with various mantra—and invariably found that words that have a meaning (like *sing, ran, sigh*, etc.) do militate against TM practice. Even another meaningless word, like, *ha*, would be undesirable: think of saying *ha, ha* as you breathe in and out—you may well begin to laugh. Then you may laugh meditation out of practice.

ERWIN DI CYAN, PH.D.
New York, N.Y.

Humanitarian Overstay

I would like to take issue with one statement in the editorial [MT, Oct. 22] which implies that "defensive medicine" plays a major role in the overuse of hospital beds. Of course we have no statistics on this subject so we must deal with impressions. I am sure that "defensive medicine" plays some role in this picture, but the major cause of hospital bed overuse, I would judge, in the area where I practice, is the overstay or hospital admission of the patient for "social causes" or "humanitarian (compassionate) reasons."

For example, the 70-odd-year-old widow who must take two buses in order to get to the doctor's office to have a barium enema done certainly is unable to do this. She must be admitted to the hospital even though it is true that this could be done much more cheaply as an outpatient under the circumstances and there is nothing in the chart that would in anyway enlighten the reviewer if he did not know the patient.

The same holds true if this 70-odd-year-old widow who lives alone should have a myocardial infarction. She would stay in the hospital far beyond the normal period because there is no one to take care of her at home. She is not eligible for the Skilled Nursing Facility for which Medicare would pay, and she cannot afford the price of even the poorest of nursing homes.

In the end, the practice of medicine is not that of robots treating robots, but of compassionate human beings trying to make life as happy as possible for our geriatric and underprivileged patients.

ARTHUR BERNSTEIN, M.D.
Maplewood, N.J.

Text of Interview: Part II

Dr. Schmidt Says M.D.s Alone Can't Decide Drug Approvals

Continued from page 1

This is used by critics to show that our labels are inaccurate, behind the times, not to be believed and so on. And this is, very clearly, a straw man that is being erected and then demolished. Because what drug labeling is for, and what the package insert is for, is to list those indications for which there is substantial evidence of safety and efficacy. And that is what we intend the package insert to convey. It is very clear that there will be new indications found for old drugs. The new indications cannot appear in labeling if there is no substantial evidence that the drug is effective for that purpose. In those cases wherein there is accumulated substantial evidence of efficacy, then, and only then, should the indication appear on the label. The reason for this is that it is equally clear that sometimes everybody will think a drug is effective for some particular use; but when the well-controlled studies are done, they will not support the popular belief. And because I would guess that in a very significant proportion of cases, a drug will turn out *not* to be effective for a condition, we should not, and cannot, list everything a drug is used for in practice on the label. That would be ridiculous. The greatest value to drug labeling is that what is on there is supported by substantial evidence.

Q. Shouldn't that point be made more clearly in the label so that the label or package insert does not become an element in malpractice suits, and juries as well as judges would clearly understand the package insert relates to claims permitted for the manufacturer of the drug and not to the control of physicians' use of therapeutic regimens?

A. Yes; I would make two points:

One is that the package insert will be and should be "behind" medical practice in some areas, because it takes time to prove, by sound clinical trials, that the practice is effective. We will shortly publish a statement that says to everybody, *"Hey, the package insert gives what is backed up by substantial evidence. There are uses for drugs that are valid, that are good, they should be employed, but if there is no substantial evidence backing that use, it isn't going on the package insert."* We will make that absolutely clear because I agree that we have the obligation to do that.

Secondly, however, I am not convinced that the package insert need be a terribly significant part of malpractice suits. When the package insert is pivotal in a malpractice suit, it is usually because the physician has not kept good records documenting the basis on which he used a drug in a manner unsupported by substantial evidence.

When I taught students how to use drugs I said, "When you use any drug, you have to keep good records and you have to record in those records the reasons you chose that drug in that dosage form for that patient's condition; and if you do that, and it is sound, you won't have to fear malpractice suits.

Q. But you would testify to the fact that the package insert is of necessity often behind the times and therefore cannot be the determinant element in a malpractice suit?

A. Again, it is not behind substantial evidence, or at least it shouldn't be, very long. It is behind the valid experimental use of some drugs. But if you go out and use a drug for an indication that is not on the package insert, you are conducting an experiment. One of the first things I said when I became Commissioner was that the physician is a scientist, and when a physician uses a drug for an unapproved indication, he is conducting an experiment. The reason he does so is that there is not substantial evidence from clinical trials that what he is doing is safe and effective. At most, he has experiential evidence of efficacy.

Q. Wouldn't you agree that because of the biological variables of patients, the treatment of virtually every individual patient constitutes therapeutic experiment in one sense?

A. Absolutely. I can go to my files and get out an old lecture I gave, and find that statement. But, you see, nobody wants the package insert to be kept up with medical practice, in the sense that any use of any drug is listed, willy-nilly.

Q. The malpractice insurance crisis raises many pertinent questions. Would you comment on how the FDA can act to improve the situation? For example, should not the bilateral adversary relationship between the FDA and drug companies on clearance of a therapeutic agent be supplemented by representation in the drug clearing process of representatives of practicing physicians as well as researchers?

A. I have said that practicing physicians should be represented in our decision-making process. That is not to say that practicing physicians alone can make the decisions, or should. In point of fact, our law and the Supreme Court agree that clinical experience alone is "treacherous," and so we come quickly back to the "substantial evidence" requirements. The scientific experiments are to be done by qualified experts. Clinical research is a specialized field, there are experts in it, and those experts as well as practitioners must be involved. We both have lived through too many things like internal mammary ligation for angina and so on to believe that clinical experience alone can be the sole judge of efficacy.

Q. You would therefore wish the FDA to regulate such procedures as experimental surgical approaches?

Vicki Lefcourt Photo

DR. SCHMIDT

A. No, of course not. I just picked what to me as a cardiologist is an example wherein individual experience can be misleading. I think it would be terribly interesting to have somebody, not the FDA, but somebody, pioneer substantial evidence requirements for surgical procedures—but we would not enjoy doing that.

Q. How do you feel about the importance of therapeutic humility in making regulatory decisions?

A. Well, one of the things we always have to do is to make a decision. No action on our part is clearly a decision. So we are asked day in and day out to answer the question, "When do we have enough evidence?" In a sense, what you are pointing out to me is that we have to be very, very careful when we are to a point of saying we do or do not have substantial evidence of safety or efficacy.

Q. How would you react to a suggestion that a rejection at any point in the IND or NDA automatically be referred to a committee, only one member of which is selected by FDA, only one by the applicant drug company, and that the two select a researcher qualified in the area of the investigation or an outstanding clinician instead of relying on the present potential administrative appeal on the part of a company? Let me just say, at present the research community and the practicing physician are not represented directly.

A. Our advisory committees see important new drugs now. Advisory committees are following new entities through the IND and NDA phases, and our advisory committees are consulted often about our decisions in open hearings. Our advisory committees include practicing physicians, academic scientists—a variety of people.

Q. What measures is HEW taking to assure drug liability coverage for generic drugs by smaller, financially less secure manufacturers?

A. The only explicit things we are exploring with other parts of the government and the White House is some means of indemnification of patients for certain kinds of experimental misadventures. But in terms of drug liability, by and large, it is our belief that it is the drug manufacturers' responsibility to manufacture a safe and effective drug.

Q. But if a small company which is virtuously without fiscal resource fails to do so, there is no way the physician or patient can be assured of economic protection in case of drug disaster.

A. If some drunk without car insurance hits me or if some small company manufacturers a product that injures my family, what you are pointing out to me is that I then may have a serious problem. I agree.

Q. But drunken driving is breaking the law.

A. So is manufacturing a drug to which the manufacturing practices do not conform with our GMPs, in which the drug does not meet USP standards, and so on. That is equally against the law.

Q. But, using your metaphor, a non-drunk driver can have an accident or a drug disaster can occur. What if a company does not have adequate fiscal strength, will the burden of that drug liability disaster fall either on the physician or on the patient under the present situation?

A. Were the patient not to have hospitalization insurance, income protection and that sort of thing, yes. If you are talking about damage suits against a negligent manufacturer, I would say yes. But that situation is similar in every economic and business area in this country. It is not unique to pharmaceuticals.

Q. But if the pharmacist can substitute for the physician's prescription, then the patient loses the economic drug liability protection usual with a large manufacturer whose drug the physician had prescribed and wanted dispensed. How can physicians and patients be protected against a drug disaster in such a situation?

A. The situation now is that liability rests with the manufacturer. Ninety-five percent of the drugs in this country are made by a relatively few number of drug firms so that the possibility you are talking about is not a great one. It is our responsibility not to regulate the industry as tightly as some are suggesting that we do, i.e., to license companies to get into the business, for example. It is still a free country and I would like it to stay that way. What we are doing is to implement procedures which, if followed, will to the extent humanly possible assure the high quality of drugs.

Q. Since present antisubstitution laws provide assurance that the patient gets what the doctor prescribes, do you see any reason for their repeal?

A. Personally or officially? Officially I won't comment because it is none of our business.

Q. In presenting side effects of drugs in package inserts, would it not be more accurate and helpful if comparable side effects occurring with placebo were listed so that the physician could make a considered judgment?

A. No, I would not think so.

To Continue Next Issue

Neurologist Pioneered Brain Scan When Radiologists Were Skeptical

Medical Tribune Report

NEW YORK—In the 29-year history of the Lasker Awards—in fact, in the history of medicine—there is nothing like the story of the work of Dr. William Oldendorf, one of the 1975 Lasker Award winners for clinical research. Nearly 15 years ago he devised and demonstrated the basic scanning system utilized in the British-created EMI scanner—and couldn't interest anyone in it. This computerized x-ray scanning system, sometimes called the CT scanner, is now considered the most important development in radiology since Wilhelm C. Roentgen's original discovery in 1895.

In fact, not until the British-made scanner began its startling revelations of brain lesions in April, 1972, did anyone pay much attention to Dr. Oldendorf, Clinical Neurologist at the Brentwood Veterans Administration Hospital in Los Angeles and Professor of Neurology at the University of California at Los Angeles. The British EMI scanner was developed quite independently of Dr. Oldendorf's work by Godfrey N. Hounsfield who shared the $10,000 Lasker Award with Dr. Oldendorf.

An engineer who adapted his experience in using radar to seek information concerning medical problems, Mr. Hounsfield now heads the medical systems section of the Central Research Laboratories of Electrical and Musical Industries, Ltd.

Questions by Medical Trubune

MEDICAL TRIBUNE published one of the first articles in the United States on the EMI scanner and its dramatic clinical revelations about lesions in the brain (MT, May 24, 1972).

Immediately after relating the history of his ignored early work in the amphitheatre at Cornell University Medical College, Dr. Oldendorf was asked by MEDICAL TRIBUNE if radiologists had been interested in his scanning concepts back in 1961 when he published them.

"Not at all," said Dr. Oldendorf, who was critical of that specialty in his prepared remarks. "I found that radiologists are not interested in anything really new. They can't think outside the usual way of doing things. If you want to talk about improving the conventional image or apparatus, they'll listen. But when you come along with something totally new—they won't listen."

Considered a Hoax or Toy

But did you present your ideas before any radiologic groups?

"Yes, I got on the program of a nuclear scanning group—twice, I think—on the West Coast. But after I gave my second talk—and showed my slides of my turntable and HO-railroad track apparatus, some fellow got up and said something like this, 'Are we really expected to sit here and take this sort of thing seriously? Is this a hoax of some sort? What is happening to this society when a fellow can put together a kind of toy and come down here and give us a lecture about it? Is this some kind of joke?' And that sort of ended it."

Industry: "No Market"

What about industry?

DR. OLDENDORF

"I went to all of them—and they all turned me down. I wanted them to develop it. But they didn't care what the machine would do. They immediately figured out that this machine would cost somewhere around $250,000 to build at that time—and that ended it. There's no market, they said, for anything that expensive. They couldn't care less about what could be visualized with it. To them, it was just a marketing problem."

Earlier, Dr. Oldendorf explained to an attentive audience that included white-coated Cornell clinicians, his fellow Lasker prizewinner Godfrey Hounsfield and Mrs. Mary Lasker, how he, a clinical neurologist, had become interested in the problem of soft tissue scanning because the physician is "required to make crucial decisions with essentially no information to work with."

Criticism of Radiology

While Roentgen's discovery revealed bony structures and solid soft-tissue lesions in the lung could be seen in contrast to aerated lung tissue, "most tissues could not be visualized" because their radiodensities were fairly uniform. The brain, which particularly concerned Dr. Oldendorf as a neurologist "was particularly invisible because the surrounding skull casts a very strong shadow superimposed on extremely faint shadows of brain tissue structures."

During the first 30 years of radiology, substantial technical improvements reduced the amount of patient irradiation, sharpened x-ray shadows, shortened exposures and improved image contrast, "but during the past half-century the technique of shadow radiography has changed almost not at all," said Dr. Oldendorf.

While an impressive mass of useful clinical correlations have been made with shadowy structures on x-rays, "in no other medical endeavor have such high level interpretations been made of such vanishingly meager data." Indeed, Dr. Oldendorf said critically, "So many subtle interpretations have been made, often highly empirically, that there has been some resistance to any change in radiographic technique lest the different appearance of the image require discarding the old established empiricisms."

The use of gas or of radiodense materials like barium, he pointed out, infer the structural shape indirectly and "the soft tissues themselves are not directly visualized. In effect, we see only where the tissues are not."

Neurologic diseases resulting in an abnormal concentration of calcium permitted a useful brain x-ray. Otherwise the x-ray was a limited tool. "We can replace the cerebrospinal fluid with gas (pneumoencephalography) or make the blood passing through the brain briefly opaque to x-rays (angiography)," Dr. Oldendorf noted, permitting visualization of the cerebrospinal fluid and the blood when one "would much prefer to see the adjacent soft tissue structures of the brain directly."

This inability to visualize the tissues of the brain prompted Dr. Oldendorf to begin work in the last 1950s on some method of achieving that goal. In a 1961 paper, he wrote: "Each time I perform one of these primitive procedures [pneumoencephalography or angiography] I wonder why no more pressing need is felt by the clinical neurological world to seek some technique that would yield direct information about brain structure without traumatizing it."

Consideration of Ultrasound

If no one else felt that need, Dr. Oldendorf did. He considered ultrasound but decided its strong reflections and refractions in passing through the skull obscured the desired internal structure detail. X-rays suffered from being absorbed by the skull to a high degree, and therefore he sought a new method of visualizing soft tissue.

Concluding that a cross-sectional scanning device was needed, Dr. Oldendorf completed his theoretical work and then built an apparatus around a

Continued on page 48

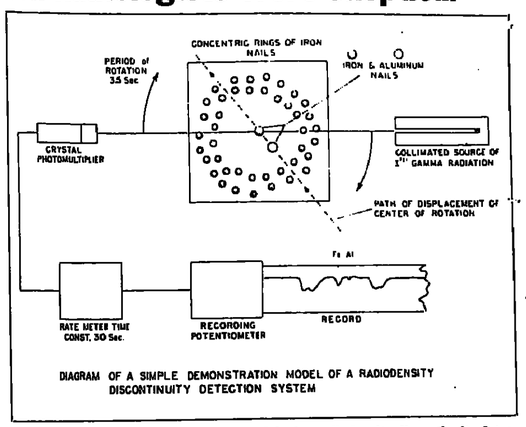
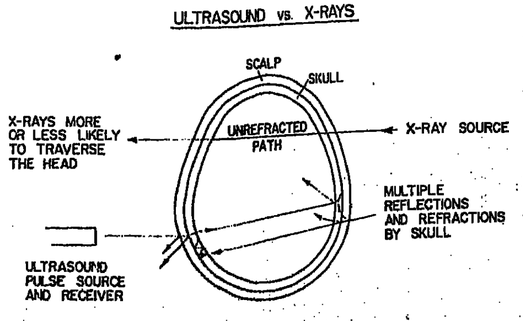


DIAGRAM OF A SIMPLE DEMONSTRATION MODEL OF A RADIODENSITY DISCONTINUITY DETECTION SYSTEM

Diagram of a "simple demonstration model of a radiodensity discontinuity detection system" shows a hardware cranial model constructed using two concentric rings of iron nails (to represent skull) and centrally placed iron and aluminum nails to represent brain structural detail. The potentiometer record defined the location and relative densities of the central nails as the point of intersection with the gamma beam moved along the path shown by the dashed line. The processing of data was much less sophisticated than is allowed by modern computerization.

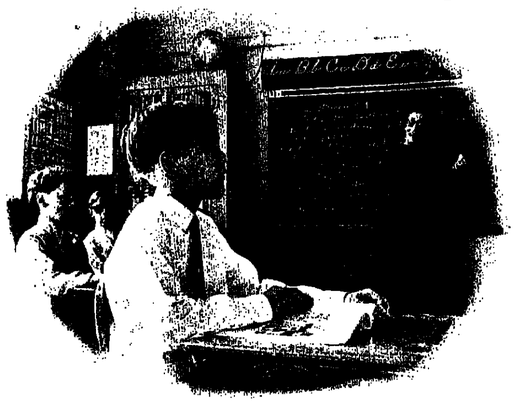


The drawback of ultrasound as a probe to define internal structure is illustrated. The narrow ultrasound beam is subject to refractions, reflections and scattering as it passes into an irregular object such as the head; the pattern is uninterpretable by current methods. A photon probe (a narrow beam of gamma rays or x-rays) passes through irregular structures without significant bending; however, x-rays are too absorbed by the skull and cannot visualize soft tissue.

Tested by time and experience in the treatment of MBD

1962

"...a considerable decrease of hyperactivity...."[1]
Knobel, 1962



Over a decade of controlled studies and clinical experience has shown the effectiveness of Ritalin in reducing the hyperactivity,[1-3] distractibility,[1,4,5] and disorganized behavior[1-8] in the MBD child.

By lessening the effects of motor and attentional disorders, Ritalin can help the MBD child to better focus his attention on meaningful stimuli and thus can often improve cognition and promote learning.[8,9]

And side effects—insomnia and appetite loss—with Ritalin have occurred less frequently than with dextroamphetamine.[10,11]

Indeed, Ritalin is currently a drug of choice in many MBD situations[1,2] and can prove to be an important element in many complete remedial programs for MBD.

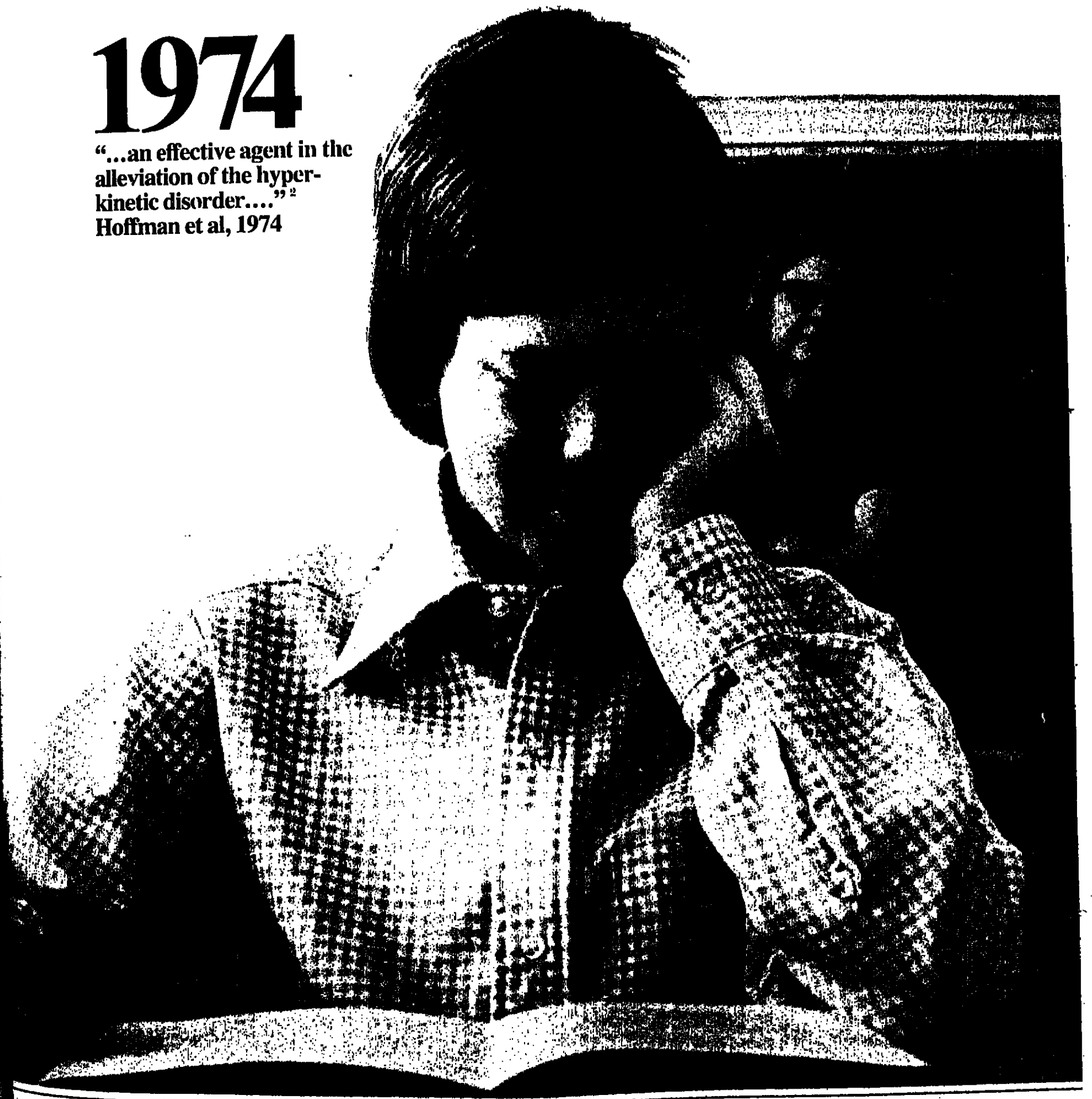
Therapy with Ritalin should be undertaken only after a medical diagnosis of MBD has been made. Drug treatment is not indicated for all children with MBD.

Dosage should be periodically interrupted. Often, these interruptions reveal some "stabilization" in the child's behavior even without medication, permitting a reduction in dosage and eventual discontinuance of drug therapy.

Ritalin®
(methylphenidate)
Only when medication is indicated

1974

"...an effective agent in the alleviation of the hyperkinetic disorder...."[2]
Hoffman et al, 1974



Ritalin® hydrochloride©
(methylphenidate hydrochloride)

TABLETS

INDICATION
Minimal Brain Dysfunction in Children—as adjunctive therapy to other remedial measures (psychological, educational, social)
Special Diagnostic Considerations
Specific etiology of Minimal Brain Dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.
Characteristics commonly reported include: chronic history of short attention span, distractibility, emotional lability, impulsivity, and moderate to severe hyperactivity; minor neurological signs and abnormal EEG. Learning may or may not be impaired. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these characteristics. Drug treatment is not indicated for all children with MBD. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psychosocial intervention is generally necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

CONTRAINDICATIONS
Marked anxiety, tension, and agitation, since Ritalin may aggravate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS
Ritalin should not be used in children under six years, since safety and efficacy in this age group have not been established.
Sufficient data on safety and efficacy of long-term use of Ritalin in children with minimal brain dysfunction are not yet available. Although a causal relationship has not been established, suppression of growth (ie, weight gain and/or height) has been reported with long-term use of stimulants in children. Therefore, children requiring long-term therapy should be carefully monitored.
Ritalin should not be used for severe depression of either exogenous or endogenous origin or for the prevention of normal fatigue states.
Ritalin may lower the convulsive threshold in patients with or without prior seizures; with or without prior EEG abnormalities, even in absence of seizures. Safe concomitant use of anticonvulsants and Ritalin has not been established. If seizures occur, Ritalin should be discontinued. Use cautiously in patients with hypertension. Blood pressure should be monitored at appropriate intervals in all patients taking Ritalin, especially those with hypertension.

Drug Interactions
Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors. Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic antidepressants (imipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Ritalin.

Usage in Pregnancy
Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing potential unless in the opinion of the physician, the potential benefits outweigh the possible risks.

Drug Dependence
Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may develop tolerance, necessitating marked increase dosage on their own initiative.
Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbance.

CAUTIONS
Patients with an element of agitation may react adversely; discontinue therapy if necessary.
A CBC, differential, and platelet counts should be performed during prolonged therapy.

ADVERSE REACTIONS
Nervousness and insomnia are the most common adverse reactions and are usually controlled by reduction of dosage and omitting the drug in the afternoon or evening. Other reactions include: hypersensitivity (including skin rash, urticaria, fever, vasculitis, and arthralgia), erythema multiforme with necrotizing angiitis (vasculitis), and thrombocytopenic purpura; anorexia, nausea, dizziness, palpitation, headache, and abdominal discomfort; blood pressure and pulse changes, both up and down; cardiac arrhythmia; abnormal weight loss during prolonged therapy. Toxic psychosis has been reported. A causal relationship has not been established. The following have been reported with this drug: leukopenia and/or anemia, a few instances of scalp hair loss, toxic hepatitis, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed above may also occur.

DOSAGE AND ADMINISTRATION
Children with Minimal Brain Dysfunction (6 years and over)
Start with small doses (eg, 5 mg before breakfast and lunch) with gradual increments of 5 to 10 mg weekly. Daily dosage above 60 mg is not recommended. If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.
If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.
Ritalin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.
Drug treatment should not and need not be indefinite and usually may be discontinued after puberty.

HOW SUPPLIED
Tablets, 20 mg (peach, scored); bottles of 100 and 1000.
Tablets, 10 mg (pale green, scored); bottles of 100, 500, 1000 and Accu-pak®blister units of 100.
Tablets, 5 mg (pale yellow); bottles of 100, 500, and 1000.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

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CIBA

FDA Chief Explains Purpose of Package Inserts

Continued from page 1

sert's role. The interview ranged over many aspects of the FDA's activities, including participation of physicians in its decision-making processes, possible use of package inserts in malpractice suits, and the problem of liability with generic drugs.

The text of the interview, the second of three installments, begins on page 1. The concluding installment will be published next week.

Asked about the misunderstandings of physicians about the package insert's role by Dr. Sackler, Dr. Schmidt cited criticism that labeling for propranolol has been criticized because it does not include hypertension as an indication. "This is used by critics to show that our labels are inaccurate, 'behind the times,' not to be believed and so on," said Dr. Schmidt. He considered this criticism "a strawman."

As he saw it, "what drug labelling is for, and what the package insert is for, is to list those indications for which there is substantial evidence of safety and efficacy."

Dr. Schmidt asserted that new indications are not warranted until "there is accumulated substantial evidence of efficacy—then and only then should the indication appear on the label." He pointed out that at times "everybody will think a drug is effective" but well-controlled studies will not support that belief.

"We should not, and cannot, list everything a drug is used for in practice on the label. That would be ridiculous."

Vicki Lefcourt Photo

Dr. Schmidt (right) told Dr. Sackler during their interview that "the package insert will be and should be 'behind' medical practice in some areas, because it takes time to prove, by sound clinical trials, that the practice is effective."

Malpractice Suits

In response to a question on the possibility of the label or package insert becoming a factor in malpractice suits and being misunderstood by laymen on a jury, Dr. Schmidt made two points. "One is that the package insert will be and should be 'behind' medical practice in some areas, because it takes time to prove, by sound clinical trials, that the practice is effective." He pointed out that the FDA will soon publish a statement to the effect that the uses for the drug on the package insert are backed by substantial evidence and that if there is no such evidence the use will not be on the package insert.

Secondly, "I am not convinced that the package insert need be a terribly significant part of malpractice suits." However; if the package insert is "pivotal" in such a suit, he said, "it is usually because the physician has not kept good records documenting the basis on which he used a drug in a manner unsupported by substantial evidence."

As he saw it, the package insert does not lag behind substantial evidence "very long."

If a physician uses a drug for an indication not on the package insert, he is "conducting an experiment," said Dr. Schmidt. "There is not substantial evidence from clinical trials that what he is doing is safe and effective. At most, he has experiential evidence of efficacy," said the Commissioner.

Dr. Sackler asked if the biological variables of patients did not create in a certain sense a therapeutic experiment?

"Absolutely," said Dr. Schmidt, citing an old lecture he gave in which he said that. "But, you see, nobody wants the package insert to be kept up with medical practice, in the sense that any use of the drug is listed, willy-nilly."

Asked by Dr. Sackler about representation of practicing physicians in the process of clearing new therapeutic agents, Dr. Schmidt said that while physicians should be represented, "clinical experience alone is 'treacherous,' and so we come quickly back to the 'substantial evidence' requirements. The scientific experiments are to be done by qualified experts."

Because Dr. Schmidt said that they had both "lived through too many things like internal mammary ligation for angina" to rely solely on clinical experience, Dr. Sackler asked the FDA Commissioner if he contemplated having the FDA regulate experimental surgery.

"No, of course, not," replied Dr. Schmidt. But he felt that it would be interesting to have "somebody—not the FDA, but somebody, pioneer substantial evidence requirements for surgical procedures."

In response to a question by Dr. Sackler about the "importance of therapeutic humility in making regulatory decisions," Dr. Schmidt pointed out that the FDA must constantly try to determine when it has enough evidence to make a decision. "In a sense, what you are pointing out to me is that we have to be very very careful when we are to a point of saying we do or do not have substantial evidence of safety or efficacy.

Dr. Schmidt said that the HEW is exploring with the White House and other parts of the government "some means of indemnification of patients for certain kinds of experimental misadventures."

However, in the FDA Commissioner's view, drug liability is the responsibility of the drug manufacturer.

If a small generic drug company, without substantial fiscal resources, fails in that responsibility, "will the burden of that drug liability fall either on the physician or on the patient in the present situation?" asked Dr. Sackler.

"Were the patient not to have hospitalization insurance, income protection, and that sort of thing, yes," said Dr. Schmidt. "If you are talking about damage suits against a negligent manufacturer, I would say yes. But that situation is similar to every economic and business area in this country."

Dr. Sackler pointed out that if pharmacists can substitute for the physician's prescribed drug, the patient may lose the drug liability protection afforded by a large company. How can physicians and patients be protected against a drug disaster in such a situation?

Dr. Schmidt did not consider this a great risk because, he said, 95% of the nation's drugs are made by relatively few firms.

Conditioning Achieves Bladder Control

Continued from page 1

sponse in spinal man which is mediated below the level of the cord lesion," he told the American Congress of Rehabilitation Medicine.

"If, as is apparently the case, the human spinal cord can be conditioned in the absence of cortical regulation to produce one type of response, urination, the question may legitimately be raised as to what other responses the isolated spinal cord is capable of learning," he commented.

Coinvestigators were Dr. Augusta Alba, associate director of rehabilitation medicine at the hospital, and Bernard S. Brucker, M.A., psychologist.

Toward Independence

The goal of the team's research was to reinstate independent voiding in patients with spastic neurogenic bladders resulting from spinal cord lesions. While electrical stimulation has been successfully employed in such patients, via the transmission of impulses to electrodes or receivers implanted in the bladder, Dr. Ince said, "because of numerous problems, including the need for surgery, post-surgical complications, the risk of infection, pain, and the necessity of having cumbersome apparatus" this technique "is neither feasible nor practical for all patients."

In the New York study, "electrical stimulation was employed as an independent variable, but unlike previous investigations, the electrodes were not internally implanted but were placed externally on the patients," Dr. Ince explained.

The subjects were two men, aged 37 and 32, diagnosed as having complete spinal cord lesions at the T3 and L4-L5 levels respectively, with no sensation below the level of the lesions. One patient was using a Foley catheter type drainage system and the other a condom drainage system at the start of the experiment.

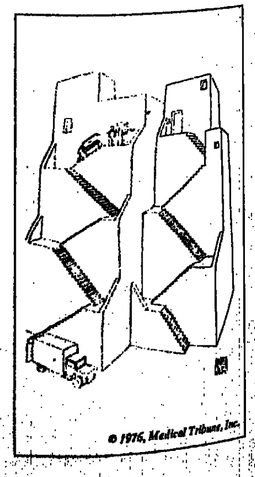
Produced Abdominal Contractions

"In order to elicit an unconditioned response (UCR) of voiding, electrical stimulation delivered to the lower abdomen was chosen as the unconditioned stimulus (UCS), "the investigator explained. "This stimulation was strong enough to produce contraction of the abdominal muscles which, in turn, increased bladder pressure and initiated voiding." The stimulation was delivered to the lower abdomen via disposable adhesive electrodes.

In a series of sessions the UCS alone was administered to establish a reliable voiding response to such stimulation prior to the "temporal pairing" of the conditioned stimulus (CS) and the UCS.

In the next phase of the experiment, a mild CS—provided by a small, handheld, battery-operated device—was applied to the subjects' inner thigh, one-half second prior to the onset of the UCS, and both stimuli ran concurrent-

Continued on page 49



Current Opinion Continued

"Uncommon Colds" and Antibiotics: Not Good Enough for President or Citizens

Continued from page 7

diagnosed) 0.14%.

It is important for the practicing physician to remember that streptococcal tonsillitis and pharyngitis, with its potential nonsuppurative sequelae of rheumatic fever or glomerulonephritis, or early purulent complications such as retrotonsillar abscess, otitis media, bronchopneumonia, etc. is a primary infection and not a bacterial complication of a viral respiratory illness. A total leucocyte count, usually over 12,000 with a predominance of polymorphonuclear cells and a "shift to the left", favors the diagnosis of acute streptococcal disease. (See Fig. 1 from Jordan, W. S., Jr. and Dingle, J. H.: Acute upper respiratory infections, *GP* 10: 49-56, 1954)

Need for Cultures

Under such circumstances it is essential to do a culture for beta hemolytic streptococci using one or another form of a "strep kit" that allows physicians to do their own cultures (see MEDICAL TRIBUNE, December 3, 1975 –INFECTION CONTROL TODAY).

The importance of doing the culture instead of mere reliance on the severity of clinical manifestations is illustrated by the studies of E. H. Townsend, Jr. and J. R. Radebaugh (Prevention of complications of respiratory illnesses in pediatric practice, *New Engl. J. Med.*, 266: 683-689, 1962) who found that only 23 of 343 "sicker" patients yielded beta hemolytic streptococci.

Dosage Levels

In the absence of early purulent complications or other clinical signs of very severe illness associated with polymorphonuclear leucocytosis, a 24-to-72-hour delay in instituting therapy while waiting for the results of the culture will not decrease the effectiveness of penicillin in preventing rheumatic fever (Jordan and Dingle, *GP*, 1954). When infection with beta hemolytic streptococci is established by culture the optimum antibiotic therapy, in the absence of penicillin sensitivity, is benzathine penicillin G (600,000 units) combined with 600,000 units of aqueous procain penicillin G in a single intramuscular injection. For penicillin-sensitive patients the less effective erythromycin is used: 20 mg. per pound of body weight per day given in four doses for a ten-day period.

The 1975 edition of "Control of Communicable Diseases in Man" an official report of the American Public Health Association (not a government agency) contains the following statement (on page 265) about *specific* treatment of acute febrile viral respiratory disease: "None. Indiscriminate use of antibiotics is to be discouraged. These valuable therapeutic agents should be reserved for *identified* [my emphasis] bacterial complications such as pneumonia, tracheobronchitis, otitis and sinusitis."

Early Diagnosis in Pneumonia

In this connection it is important to remember that pneumococcal pneumonia is an acute disease of sudden onset with a well-defined clinical syndrome in which an early *etiologic* diagnosis is important for *proper* antibiotic therapy. Although the demonstration of *many* gram-positive diplococci in smears of lower respiratory tract sputum can constitute a presumptive diagnosis, confirmation by culture of sputum and blood is essential. Bacterial pneumonia, other than pneumococcal, most often occurs as a superinfection associated with viral infection of the respiratory tract, broad spectrum antibiotic therapy, chronic lung disease, aspiration of gastric contents, tracheostomy. Different bacterial agents are involved and *successful* therapy depends on identification of the organism and its antibiotic sensitivity (see pp. 235-236 in "Control of Communicable Diseases in Man").

Role of Tests

It is also important to remember that not all pneumonia, tracheobronchitis, and otitis is caused by bacteria and that the patient is best served by determining the presence or absence of polymorphonuclear leucocytosis combined with proper bacterial cultures and antibiotic sensitivity tests. So-called "sinus congestion" or post-nasal drip can hardly be regarded as clinical indicators of a complicating bacterial sinusitis, but more serious clinical manifestations such as purulent discharge coming from the ostia of the involved sinuses, pain and tenderness on pressure over affected sinuses, anosmia, vertigo, toothache, etc. associated with fever and malaise require a white blood count and bacterial cultures.

Dr. Sackler concluded his Nov. 19 article as follows:

"Until we hear from you, out there, may I close with a heartfelt observation: *What's good enough for the President of the United States is good enough for our patients, the citizens of the United States."*

In my judgment the data that I have referred to and summarized here provide answers to the *questions* posed by Dr. Louis Lasagna and indicate that the way antibiotics are currently used in acute respiratory illness by many physicians is not good enough for either the President or the citizens of the United States.

Testicular Cancer

Medical Tribune Report

INDIANAPOLIS—Combined chemotherapy with velban, bleomycin, and an investigational drug, cis-diamminedichloro-platinum (II), has resulted in complete 18-month remission in 75% of 20 patients with testicular cancer, according to Dr. Lawrence Einhorn, chief of the chemotherapy section, department of medicine, Indiana University School of Medicine. However, this is a "rough regimen" with acute side effects requiring careful monitoring and "not for patients whose cancers can be excised," he told a postgraduate seminar jointly sponsored by the IU and the American Urological Association.

A Story of Human Courage

JOSEPH JOHN DEACON, left, a spastic at St. Lawrence's Hospital, Surrey, England, recently completed his autobiography, *Joey*, with the painstaking assistance of fellow-patients Tom, Ernie, and Michael (l. to r., below). Published by Charles Scribner's Sons, *Joey* serves to awaken normal readers to the wonder of simple transactions—walking, using one's hands, being understood. The book, suggests Consultant Psychiatrist Geoffrey Harris, "will encourage us to listen with proper humility." Joey writes simply: "I thought to myself, if only I could make myself useful; if only someone up above could give me the power to do the things I wanted to do. Then I thought, oh well, you can't have all the luck."

Tomography Favored in Diagnosis of Seizures

Medical Tribune Report

CHICAGO—The safety and diagnostic accuracy of computerized tomography (CT) make this scan "the radiologic procedure of choice" for initial evaluation of patients with seizure disorders, investigators from Hahnemann Medical College and Hospital reported here.

Studies of 464 patients with a history of seizures demonstrated that 30% had abnormal CT scans, Dr. Patricia Laffey told the Radiological Society of North America.

As could be expected, the 66 patients showing focal abnormality on clinical examination had a high overall incidence of CT abnormality—63.6%, with a 24% incidence of tumor.

Dr. Laffey emphasized, however, that 96 of the 398 patients who were otherwise asymptomatic also had abnormal scans, with a 3.5% incidence of tumor.

Generalized atrophy proved to be the most common abnormality, detected in 60 of the 138 patients with abnormal CT scans. Next in frequency was tumor, found in 22 members of this group. A diagnosis of porencephaly was reached in 12 patients and infarction was observed in the same number.

Evaluation of patients according to age made it clear that the incidence in abnormal scans rises with increasing age in patients with seizure, Dr. Laffey said. For example, among the entire group of 398 considered normal on physical examination, the percentage with abnormal CT scan rose from about 5% in those under the age of 20 to twice that level among young adults (aged 21-30), and to 63% in patients aged 50 or older.

Citing the advantages of computerized tomography in evaluating the patient with seizures, Dr. Laffey pointed out that the technique has a diagnostic error rate of only 3 to 4%, and can be performed on an outpatient basis with consequent savings in cost.

The safety of CT scanning is another —and major—advantage, in her opinion, since the examination is noninvasive and thus entails no hazard to patients.

Coauthors included Drs. Carlos F. Gonzalez, Marvin B. Haskin, J. George Teplick, and Bruce M. Bogdanoff.

Janeway Answers Questions

One of the nation's leading economic consultants, Eliot Janeway, regularly answers questions raised by MEDICAL TRIBUNE *readers in his weekly column.*

A financial writer I sometimes read said that interest rates have to be high during inflationary times. But you have said, "A period marked by a higher rate of inflation, reflected in high interest rates, is no time to hold long term bonds.' I feel you're disproven by the drop in interest rates despite inflation. Am I wrong?

Suburban Long Island M.D.

Yes, you are. The drop in interest rates coincided with the spate of publicity about inflation slowing down. This publicity has now been proven wrong. The bond market always runs on a short fuse. I expect interest rates to rise again.

If I buy a tax-free municipal bond with the same interest rate as a corporate bond, should I place it in my Keogh retirement shelter?

Chicago Surgeon

There's no need to waste tax-sheltered income by putting it in tax shelters—and no point in trying.

My wife and brother-in-law are really uptight about our economic system, government, etc. In 1974 they took off over silver, after Harry Browne published his book, and so scared me about everything on paper—including paper money—that I jumped in and bought silver because the dollar was failing. I had a 3 to 1 margin. Then last July silver slumped and I gave up half my silver to meet the margin call. But right now I'm sitting still and paying $140 a month in interest and charges to hold onto a so-called precious metal that certainly seems to be a dead-end or worse. Should I just admit my foolishness, take my loss and get out?

Florida Urologist

Absolutely.

My wife and I have $25,000 in utility stocks paying about 12%, $11,000 in certificates of deposit at 7%, and $6,000 in a savings bank. I'd like to return to a small town and go into general practice, even though it would mean a financial sacrifice. But with the money that's available now, should we buy more stocks, more CDs, or keep everything as liquid as a Treasury bill?

San Francisco Internist

Keep everything as liquid as a Treasury bill in spite of current loss of income.

I am soon to retire from general practice, age 65. I have $120,000 invested in Treasury notes and AAA long-term corporate bonds. I also have $15,000 in a savings account and will receive $9,600 from Social Security and my Keogh plan, giving me a total income of about $20,000. I have been thinking of buying a retirement home, but the one I want costs $40,000. As I see it, I'd make a $10,000 down payment. Is my income going to be sufficient? Should I figure on doing some consultations?

Tired M.D., Western Pa.

Never figure your income will be adequate. By all means, keep your hand in and charge for the work.

I am age 41, have been incorporated for one year, and have accumulated about $15,000 in corporate bonds paying about 9½% in my pension and profit sharing plan. Should I continue to buy these bonds or hire an investment managing firm?

Kansas M.D.

As long as you're going for bonds, why settle for a mere 9½% rate? At your age, in your income bracket, you can afford some risk. If, for example, you were to accumulate utility preferred stocks yielding over 11% you would be running no risk of default and you could bank on a profit sometime during your likely working career.

With $15,000 in your fund, you do not begin to have enough to afford an investment managing firm.

In your column of November 5th, you advise the Medical Couple against investing in utility bonds and long term Treasury bonds. Would you give the same advice to one who is already retired for more than a year? I'm 80 years old and my wife is 77.

My bonds, mostly double and triple A, consist of $50,000 short term and $86,000 long term. I also have about $100,000 in stocks, most of which are 10 to 20 years old, and an equal amount in cash.

Boston M.D.

The older an investor is, and the less the life expectancy, the greater the incentive to concentrate on maximizing current income and to ignore the possibility of interim paper losses on fixed income securities during the next few years.

Your letter does not indicate whether you own insurance. Your wife is younger than you are and would be exposed to market losses in the event she survived you during any interim period of market setback. With your cash and portfolio reserves, you could afford either to go for more income than bonds could pay you by switching to utility preferred stocks or to tax exempts.

Have you given thought to taking profits in your stock portfolio? Doing so would take the risk out of owning high yielding bonds or preferreds. You could use future losses from them to offset profits on your stocks, meanwhile increasing your income.

Having purchased a considerable sum of N.Y. State Bond Anticipation Notes maturing June 15, 1976, I am quite concerned about their safety especially as I had planned to use them for estate taxes for my mother-in-law who is terminally ill and given three months to a year to live.

Shall I sell now—and what loss would be incurred—or should I ride it out?

Concerned Pediatrician

I am sorry for your sake you took so long to ask me about your New York State Bond Anticipation Notes. I've been warning about them for many months. The decision to sell is easier than finding a buyer for anything with New York State's name on it. I do not regard them as businessmen's risks, and think you will be well out of them.

What would you advise one with a pacemaker, age 61, who is still practicing but thinking of retirement because of disability to do with his money? I'm already in a growth fund and an income fund. If I shouldn't continue to practice, what investment media would you recommend?

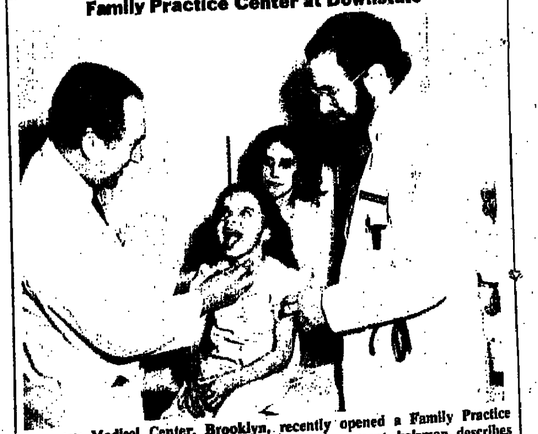
South Carolina M.D.

Growth funds would not be appropriate for you in your circumstances, even if they were still doing well. If you do opt for retirement, you will want to maximize income. Meanwhile, liquidate your growth funds.

Ask Janeway

Send your questions on finances, investments, taxes to Janeway, MEDICAL TRIBUNE, *880 Third Avenue, New York, N. Y. 10022.*

Family Practice Center at Downstate



Downstate Medical Center, Brooklyn, recently opened a Family Practice Center which Dr. Charles M. Plotz, above left, department chairman, describes as "not a clinic for the treatment of a single type of illness, but a group of family doctors working together." The new center should answer a growing local need for "old-fashioned medical care—treatment of the whole person and not just a specific ailment."

Scan Pioneer Followed American Tradition

Continued from page 41

hardware model of the cranium and cranial cavity. A collimated narrow beam of gamma rays was passed through the model to a detector. The cross-sectional plane was examined by spinning both the gamma ray source and detector about an axis of rotation which intersected the narrow beam.

Moving Intersection Point

The intersection point was moved along a line within the plane being examined. The material at the intersection contributed a constant or DC component to the absorption of the beam while all other material in the plane (but not at this intersection) was only intermittently exposed to the beam. This caused the intersection material to be heavily weighted in its effect on absorption of the beam as compared to all other regions in the plane being swept. As the intersection region moved along a line within the plane, changes in density would modulate the intersection DC component at frequencies below any modulation due to discontinuities elsewhere in the same plane. The count-rate of the emerging gamma beam could then be analyzed. In this way, a series of points in the plane could be isolated, examined and displayed independently of all other points in the plane.

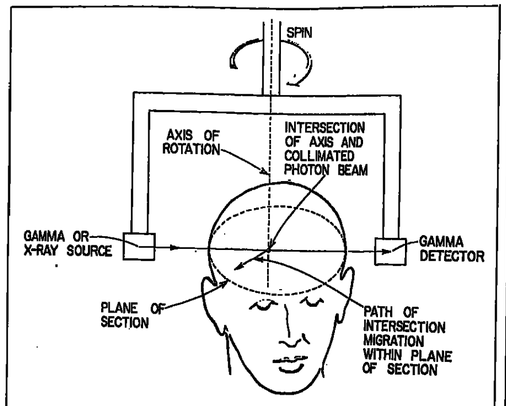
However, because moving both the gamma ray emitter and its detector was cumbersome, Dr. Oldendorf decided to build a new apparatus in which the beam would be kept stationary. He made a phantom "skull" by driving about 40 iron nails in two irregular concentric rings in a block of plastic. Then he drove two nails—one iron, the other aluminum—into the center of these rings—symbolically representing the lesion within the cranial cavity. He wanted to determine if this simulated intracranial detail could be demonstrated within the surrounding skull.

The "skull" was then placed on a turntable. This permitted rotation of the "skull"—and the passing of a single line of gamma ray photons through the outer iron and aluminum nails. Thus their positions and relative densities could be displayed (see diagram).

Problem of Tissues

At the time, Dr. Oldendorf secured tracings that clearly indicated the inner and outer rings as well as the inner "cavity" nails. However, as he was well aware, it was one thing to secure such a display of large density differences, with an iron nail and an aluminum one, and quite another to gain similar results with living tissues. As he put it, "There was no assurance that the very slight differences existing within living structures would be visible. The ability to detect slight differences in density is determined by statistical fluctuations due to the finite number of photons that can be generated and passed through human tissues."

Whether this was practical was difficult to tell. "To obtain clinically useful information could well have required a megawatt of power dissipation to produce the x-rays, scan times of hours per section, and a destructive level of tissue irradiation," Dr. Oldendorf told the audience at Cornell.



The basic principle of transmission scanning tomography, as formulated by Dr. Oldendorf in 1961, is illustrated. A plane through the head was "swept out" by a moving high-energy photon source and mechanically coupled detector. The axis of rotation intersected the beam's path. This intersection point was moved through the plane and the absorption of the beam by the material occupying this point was electronically isolated from other points in the plane.

However, none of these questions ever came up because the five major x-ray firms he approached held that "no viable market could exist for such a complex device which did nothing but produce a cross-section of the head. Therefore, any discussion of its technical feasibility was superfluous."

Abandonment of Work

Dr. Oldendorf did patent his device but by 1963, after a few more discouraging meetings with clinical groups interested in scanning, he stopped work and abandoned his efforts to gain support for a clinical apparatus.

Meanwhile, working quite independently, Godfrey Hounsfield of EMI, Ltd., "developed a method for producing radiographic transmission section scans having a number of features in common with my earlier method," Dr. Oldendorf said. In the EMI apparatus, all of the points in the plane of interest were examined by a collimated narrow beam of photons using a combination of linear and rotary motions.

But Hounsfield utilized a more advanced method of computerization and he was able to demonstrate that "a reasonably sized x-ray source" could produce the needed photons, resulting "in a tissue exposure approximating that produced by a single shadow radiograph of the head."

Even though the cost of the apparatus is $400,000, "the EMI scanner, like all good products, sells itself," Dr. Oldendorf pointed out, rebutting the idea that there was "no market" for such an instrument. "Hospitals have willingly paid the price because the clinical information the device provides is so great and this information is obtained atraumatically."

New Applications in Soft Tissue

Dr. Oldendorf concluded by pointing out that computerized scanning tomography will greatly advance physicians' ability to manage ill patients. Applications of the device are being made in all areas where soft tissue has previously made it impossible to visualize lesions. "It should produce results as revolutionary as were those in the brain," said Dr. Oldendorf. "Many of the answers to questions about the characteristics of diseased tissues which physicians previously found only at the autopsy table can now be obtained in the patient while still alive."

Dr. Oldendorf told MEDICAL TRIBUNE that he expects neurology and radiology to be influenced greatly by these new applications of computerized scanning tomography.

Lung Lesions Laid To Asbestos Fibers Borne by Air

Continued from page 1

Asbestos is not easily degraded, hence its popularity in industrial use. Once in the environment, the fibers tend to remain. The cumulative environmental burden is estimated to be about 2.5 million tons a year.

The ten cases were picked up among U.S. Navy personnel receiving periodic physical examinations. None were shipyard workers with frequent exposure to asbestos. Their exposure was not considered significantly greater than that encountered by the average urban worker.

All were in their late 30s to 70s with the peak incidence of onset in the fifth decade. The thickenings were bilateral in eight individuals. In a few, thickenings were extensive, suggesting mesothelioma. But the clinical significance of these findings cannot be evaluated at the present time, said Dr. Ochs, whose scientific exhibit at the meeting showed pleural hyalinosis along the posterolateral parietal pleura.

IMMATERIA MEDICA

A Bad Year 50 Years Ago

In celebrating the awarding of the Nobel prizes to Drs. Howard Temin, David Baltimore and Renato Dulbecco, the British magazine *New Scientist* went back and looked up who got the prizes 50 years ago. And it turned out that nobody did. As the *New Scientist* put it, "1925 was a bad year for biology. . . ."

Football Positions Defined

From Dr. H. B. Grainger, of Tyler, Tex., the following:
Corner Back: acute kyphosis
Split End: spina bifida
Running Back: dorsal hyperhydrosis
Tight End: fissure in ano
Tailback: coccyx
Wide Receiver: steatopygous receptionist.

Anyone for Massage Defining?

Dr. Milton H. Erickson, now of Phoenix, Ariz., who has been practicing psychiatry a long time, has forwarded a postcard from a former patient [name deleted]. It reads:

"Dr. Erickson: I was desperate for someone to talk to a few days ago (by the way the only reason I am unhappy is that I need someone to talk to. It is not because I don't have a job. I have had the same job for a year now) that I went to a massage parlor and paid to talk to one of the girls. She explained to me in very simple terms why I don't have a girl friend. I scare them away by asking too much from them and I don't show them affection properly. Why couldn't you have told me this when I was seeing Gladys [false name inserted] years ago. I need a smart girl. [Signed].

Writes Dr. Erickson: "After 46 years I have discovered a major deficiency in my psychintric armamentarium. It does not comfort me that this patient has found the same deficiency in many of my Phoenician colleagues. I do emphasize that the present campaign by the police against massage parlours does not signify a conspiracy between psychiatrists and the police.

"Parlours may be spelled as parlors but as yet there has been no clear definition of massage.

"Struggling to keep up with medical advances."

Clinical Cliché

"Blood loss was arrested."

Method Achieves Bladder Control In Spinal Injured

Continued from page 44

ly, terminating simultaneously. The CS had a total duration of three seconds, the last two and one-half seconds of which was paired with the UCS.

Dr. Ince pointed out that prior to both UCS stimulation alone and UCS-CS pairing, the CS alone was applied during two sessions of 15 trials each "in order to establish the neutrality of the CS."

Effect After Pairing

In the penultimate phase of the study, CS trials were conducted in order to determine the effect of the CS, after pairing, on the voiding response. In the final phase, once the CS had been established as an effective stimulus for eliciting urination "a shaping procedure" was carried out, according to Dr. Ince.

"At first, th subjects pushed up from their wheelchair seat fully, arms extended. Then gradually, they pushed up less and less, during each session, until finally, they were seated during stimulation. In addition several trials were conducted where the subjects sat on a bedpan or a toilet while receiving the CS. Once the subjects were voiding while seated, they administered the CS to themselves. Each subject self-administered the CS on all trials for five sessions. Self-administration of the CS was also performed when they were on the bedpan or toilet," he said.

Results in one subject showed that "the percent of successful responses elicited by the CS alone remained the same (71%) as that of the UCS and pairing sessions. This indicates that the CS, a previously established neutral stimulus, was now eliciting voiding responses at about the same rate as the UCS," the investigator reported. During the shaping procedure, a response rate of 38% was achieved in that patient.

UCS successfully elicited a voiding response in the other subject, during catheter drainage, 65% of the time, and in paired trials 70% of the time. In CS alone trials, an "extremely successful rate of responding (85%) was elicited by the previous neutral CS," Dr. Ince reported. After the catheter was replaced with a condom drainage device and the CS alone was applied, no voiding response was obtained and the entire experimental procedure was replicated with patient on condom drainage, whereupon basically similar results were obtained as in the other subject.

"A feature of all conditioning techniques," Dr. Ince cautioned in discussing the results, "is the process of extinction. In the case of classical conditioning, which was employed in the present investigation, extinction, or the gradual decline of responding, occurs when the CS no longer is paired with the UCS for a period of time.

Extinction Uncertain

"Both subjects in the present study," he continued, "were discharged from the hospital before extinction would ordinarily begin. Whether or not extinction would have occurred had the experiment continued for a longer period of time is uncertain because of the uniqueness of conditioning spinal man.

"For the same reason, the final goal of the study—independent bladder functioning—could not be attempted. However this research is ongoing."

Commenting on the theoretical implications of his work, Dr. Ince said, "It is of significance that conditioning was achieved in the absence of brain regulation. It is the first such instance involving human subjects. Until this time, cognition had been considered essential for any conditioning to take place. However, since both subjects had a complete transsection of the cord, cognition is ruled out as an intervening variable.

Reflex Arc Involved

"Precisely which physiological responses were conditioned is difficult to determine from the data. It is the impression, gained from this study and present research, that it is the reflex arc in the sacral portion of the spinal cord which is involved with micturition which is the dependent variable. Since the CS does not produce abdominal contractions while eliciting the CR, it is most likely not abdominal musculature nor its consequent effects on intravesical pressure which are responding. It is also unlikely that the sphincters are functioning independently in response to stimulation. Further research is being directed at this question," he stated.

Clinical Trials

By Oldden

TRIBUNE SPORTS REPORT

Padding, Prompt Care, Rest Averts Myositis Ossificans

Medical Tribune Report

ANN ARBOR—Myositis ossificans or localized non-malignant heterotopic bone lesion, one of the more disabling conditions facing the athlete, can be prevented by adequate padding, prompt treatment of contusions and total inactivity, according to a Cleveland orthopedic surgeon.

"The best treatment is prevention," Dr. H. Royer Collins told a symposium on the knee in sports sponsored by the American Academy of Orthopaedic Surgeons and held at the University of Michigan. Dr. Collins is head of the section on sports medicine at the Cleveland Clinic Foundation in Ohio.

Two to four days of rest, with or without immobilization, immediately after the injury, along with ice and compression is recommended therapy.

"This means that in direct opposition to the beliefs of many people, 'charlie-horses' should not be run out," declared Dr. Collins. "They should be rested and allowed to resolve spontaneously.

"Passive physical therapy is the greatest single taboo stressed in preventing myositis ossificans traumatica. Massaging, rubbing, or any passive range of motion exercises should not be allowed. Passive exercise delays maturation and probably contributes to a larger lesion."

Myositis ossificans can occur in almost any muscle or muscle group in the body although most commonly it appears in the quadriceps muscle of the thigh or the brachialis of the arm. "This ectopic bone formation most often results from direct trauma in which the muscle and the connective tissues have been abruptly compressed against the bone, or in which tendons or fascia have been avulsed from their bony attachments," said Dr. Collins.

Secondary injury to soft tissue occurring as a complication of hip dislocation or any fracture needing multiple attempts at reduction, has also been associated with myositis ossificans, he added.

Muscle Replaced

"One important point to realize is that the tissue that becomes bone is not the bruised muscle itself," Dr. Collins stressed. "The new bone is formed from primitive connective tissue and pluripotential mesenchymal cells. The injured muscle is replaced, not transformed."

Clinically the athlete presents with pain, swelling and limitation of motion. There is usually a history of a direct blow to the area. A palpable mass may be detected several days later. Associated knee injury and bleeding at the contusion site should be ruled out as causes of swelling, Dr. Collins said.

X-ray evidence of myositis ossificans shows up two to four weeks after injury. The mass either dissolves, depending on its size and location, or gradually progresses to true heterotopic bone formation.

X-rays of thigh area show periosteal type of myositis ossificans, in which the periosteum separates from the bone during trauma. Evidence of lamination of periosteal new bone may simulate a primary osseous malignancy.

Studies indicate myositis ossificans usually develops in cases of moderate to severe contusion, according to Dr. Collins. Patients in this group are unable to flex the injured knee more than 90 degrees.

The three types of myositis ossificans —parosteal, periosteal and extraosseous —are differentiated by radiography. Parosteal, the most common, involves a lesion near or against the shaft of a long bone and shows up on X-rays two to three weeks after the injury, said Dr. Collins.

Myositis ossificans is sometimes confused with sarcoma, Dr. Collins noted. In periosteal myositis ossificans, the periosteum separates from the bone during trauma. "Roentgenograms show evidence of lamination of periosteal new bone which may simulate a primary osseous malignancy," he said. Initial biopsy evidence may also be confusing.

However, the two can be differentiated three to four weeks after injury by several histologic features: cellular and mitotic activity at the lesion's periphery are greater in sarcoma; there are more fibrous tissue and bone in myositis ossificans; and the benign process does not invade adjacent tissues or blood vessels.

Hyaluronidase Used

In addition to complete rest, hyaluronidase by direct injection has also been used in therapy. "But there are not enough data available to draw any valid conclusions regarding this form of treatment," said Dr. Collins.

"When myositis ossificans traumatica has already developed," he continued, "treatment is the restoration of motion and strength with protection of the area of ossification with specially made fiberglass pads."

Surgery to remove the bone should only be performed when the mass is extremely large and in a region subjected to repeated trauma or if it creates a handicap by restricting joint motion. However, "there is no guarantee that the operative treatment will be successful and therefore, if the mass is not bothering the patient, the lesion should not be excised," Dr. Collins concluded.

Seminal Sperm Marker Gives Clues in Rape Cases

Continued from page 3

The genetic differences found in the sperm of the 55 donors were based on variations in the patterns of another enzyme, diaphorase, which also differed from patterns of the same enzyme found elsewhere in the body. Two of the enzyme patterns are shared by something less than half of the 55 sperm donors, with seven showing the third variation.

Although the sample was too small to extrapolate the findings to the entire population, Dr. Sensabaugh believes that it would be very useful if prosecutors could show the racial identity of a rapist based on immunochemical characteristics in the sperm.

In addition, the Berkeley scientists have extended their genetic profile to include other substances which are not found in the sperm or semen alone, but which also vary in the sperm and other tissue of different individuals. These include esterase D, amylase, glutathione reductase, and thirteen others. Five of the genetic markers are found in the seminal plasma, seven in sperm and three are found in both sperm and seminal plasma. Taken together, the Berkeley findings suggest that it is now possible to distinguish semen samples from two individuals with a probability of about 95%, Dr. Sensabaugh said.

wine talk

By JOHN CHAMBERS
Author and Consultant to Morrell & Company, New York Wine Merchants

Champagne: The Wine for Celebration

Champagne and celebrations: the two are inseparably linked. Champagne itself is a kind of miracle. For centuries the producer of rather tart white wines and reds that were too light, the Champagne region of France took a new lease on life with the invention of the bottle cork. Now that sparkle that had appeared naturally with the renewal of fermentation in the Spring (after a long, cold winter had halted the initial fermentation) could be trapped and expanded upon. Many refinements followed, including the use of stronger bottles, the invention of the *riddling rack* to aid in the process of bringing the sediment to rest against the cork, and the process of *disgorging* to remove the sediment with a minimal loss of wine. The result is true French champagne as we know it today: distinctive, elegant, much imitated, never equalled or surpassed.

The basic champagne on the retail shelves is non-vintage *brut*. This will be the driest champagne of the producer, blended from a combination of red and white grapes to conform to a traditional "house style." *Vintage brut* will be equally dry, but reflecting the quality of a particular harvest, it will often be a little more full-bodied and/or a little more elegant. *Blanc de blanc* champagne, increasingly popular, is made only of white grapes and is the lightest and most delicate Champagne.

Paradoxical 'Extra-Dry'

Extra-dry champagne belies its apparent meaning by providing a hint of sweetness, while *sec* and *doux*, rarely seen in this country, are outright sweet. *Rose* champagne is essentially *brut* nonvintage with a tinge of pink—a festive touch. Finally, there are the *prestige* champagnes, led by the *Dom Perignon* of Moet or Chandon. Each company has one of these, and it represents the finest vintage *brut* available from their wine stocks: in short, the best.

Many other sparkling wines are produced in the world, and most of those which you will encounter on the retail shelf represent good value. I recommend especially the *vin mousseux* (sparkling wines) produced elsewhere in France. Names to look for are *Le Duc, Kriter*, and from the Loire Valley, *Bouvet Brut, Blanc Foussy*, and *Sparkling Vouvray*. The sparkling wines of Germany, of which *Henkell Trocken* is the most widely available, offer just a hint of sweetness. California and New York champagnes are increasingly good. Brands I would recommend are: Korbell, Kornell, Gold Seal, and Great Western. Finally, there are the *Asti Spumantes* and *Lachrima Christis* of Italy. These are dessert wines. All in all, they add a festive touch which no other beverage can match; a miracle forever reborn.

Injectable Contraceptive May Be Marketed

Continued from page 3

normal cancer rates Rep. Fountain had cited, and another presented by a scientist from the Upjohn Company, the drug's manufacturer.

Mr. Litt said that data from the National Cancer Institute's third epidemiologic survey were adjusted to a group of 2,908 women who had been taking medroxyprogesterone acetate and that cumulative rates of cervical carcinoma in situ were then calculated through the third year of exposure. The major finding in this study was that the incidence of the cancer increased among the drug's users as time went on, particularly among whites.

The Upjohn representative concluded that the higher reported incidence of carcinoma in situ among medroxyprogesterone acetate users was due, among other things, to the fact that they had more disease at the time they entered the various studies. He also noted that such possible risk factors as age of first coitus among older patients, sexual history, and the effects of their socioeconomic status had not generally been taken into account.

After various formal and informal meetings at which it heard reports by several pathologists, the joint ad-hoc subcommittee concluded that because of inadequate data, it was impossible to determine whether medroxyprogesterone acetate use as an injectable contraceptive can be related to the development of cervical neoplasia.

In its recommendation to allow the limited and controlled marketing of the drug, therefore, it also suggested that more variables be included in research protocols and that pathology specimens be evaluated without foreknowledge of treatment.

Two Eggs Per Day

Medical Tribune Report

LOS ANGELES—Two eggs a day probably will not affect blood cholesterol levels in normal persons, according to Dr. Grant Slater of UCLA. Healthy male subjects showed no significant changes in blood cholesterol levels prior to or during a diet of two eggs per day in addition to usual intake.